



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Victor Raso
Application No.: 09/992,994
Filing Date: November 6, 2001
Title: IMMUNOLOGICAL CONTROL OF β -AMYLOID LEVELS *IN VIVO*
Art Unit: 1652
Examiner: Patterson, C.

DECLARATION OF KATHLEEN G. MORGAN, Ph.D.

Commissioner for Patents
PO Box 1450
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Dear Sir:

I, Kathleen G. Morgan, Ph.D., do hereby declare and say:

1. I am a Professor and Chair of the Department of Health Sciences at Boston University's Sargent College of Health and Rehabilitation Services.
2. Until 2007 I was a Senior Scientist, with tenure, at the Boston Biomedical Research Institute (BBRI). I first joined BBRI in 1992 as a Consultant. I was elected a Corporator of BBRI in 1994 and became the Director in 1995. I served as Director until 2001.
3. When I became Director, I instituted a review of the BBRI's financial condition. The BBRI is an independent, not-for-profit biomedical research institute. As such, it is dependent upon federal grants, principally from the National Institutes of Health (NIH),

for its revenues. The typical NIH grant received by BBRI (“an RO1”) provides the BBRI with direct costs for the research project (salaries, supplies, etc.) and indirect costs (overhead costs, such as light, heat, administrative services, etc.) [Ex. A at p. 7]. With few exceptions, the salaries of BBRI faculty are paid by such grants as direct costs. BBRI faculty are expected to be self-funded, generating their income via such grants.

4. While the BBRI depends upon grants to pay faculty salaries as direct costs, such grants are also very important to the BBRI because they fund the overall budget as indirect costs. Otherwise, the grant would not reimburse BBRI for the overhead cost associated with a particular project [Ex. A at p. 4].

5. Because BBRI faculty are expected to be self-funded, they are expected to generate new grants regularly. When I became Director of BBRI, however, five faculty members had no funding and were “non-performing.” [Ex. B at p. A-17]. As Director, I instituted a new Strategic Plan and accompanying policies to address this and other financial issues. The Strategic Plan was approved by the Board of Trustees in 1996.

6. These changes resulted in several non-performing faculty members leaving the BBRI over the next several years. Specifically, we let go several faculty members who did not have funding [Ex. B at p. A-21].

7. We also moved several faculty members who had no funding to non-salaried positions and provided temporary funding to faculty members whom we thought were likely to regain funding [Ex. B at p. A-22]. This Bridge Support had previously been awarded on a somewhat *ad hoc* basis, and we standardized the program. The new policy made clear that Bridge Support was available for only one year, other than in “exceptional circumstances.” [Ex. C at p. E-06]. The primary criteria for determining

whether such an exceptional circumstance existed is the probability of funding [Ex. C at p. E-06].

8. The changes we instituted achieved their goal. The BBRI significantly increased its grant base [Ex. D at pp. 2, 3]. As would be expected, however, non-performing faculty members were not pleased with the changes. In 1995, no faculty members left the BBRI [Ex. B at p. A-11]. In 1996, four faculty members left the BBRI; in 1997, five faculty members left; and in 1998, four faculty members left. Departures were a combination of non-performing faculty departing the Institute and successful faculty being recruited away to premier Boston universities and industry [Ex. B at p. A-11]. At the same time, we instituted an aggressive recruitment program to hire faculty that were likely to be more successful in generating funding [Ex. B at p. A-22].

9. When I presented the Strategic Plan to the faculty, Vic Raso approached me and inquired about tenure. BBRI faculty hold appointments of three, four, and five years for Scientists, Principal Scientists, and Senior Scientists, respectively [Ex. C at p. B-06a]. Reappointment to an additional term is dependent upon four criteria. The primary criteria is grant support [Ex. C at p. B-03]. In certain cases, however, BBRI would award tenure to faculty members, resulting in a permanent appointment [Ex. E at p. 4]. Vic was untenured and had no funding at that time, so he must have recognized that the changes we were instituting would jeopardize his job security.

10. Vic actually was already on Bridge Support when we instituted the new policy. He requested a second year of Bridge Support in late 1996. In support of his request, he indicated that he was actively working on five different grant applications [Ex. F at p. 1]. Although he did not appear to meet the new criteria for Bridge Support, BBRI

approved further Bridge Support, although for only eight months, not a full year [Ex. G at p. 2].

11. Vic continued to seek funding. His many and repeated efforts were not successful, however. Vic even tried to obtain other sources of funding, seeking Small Business Innovation Research Grants (SBIR), as well as grants from the Alzheimer's Association. Having failed to get the typical NIH grants, Vic tried these sources, even though he knew the BBRI was not terribly interested in such grants. Indeed, Vic was a member of the Committee on Research (COR) that voted to grant further Bridge Support to a faculty member [Ex. G at p. 1]. That vote was contingent on the faculty member obtaining NIH funding. The COR specifically stated that "an Alzheimer's [Association] grant would not be enough." [Ex. G at p. 1].

12. Vic continued to fail to obtain funding. Therefore, in September 1997, I formally warned him, pursuant to the BBRI's Faculty Reappointment Policy, that he might not be reappointed as a Senior Scientist when his term ran out in two years [Ex. H]. I indicated that his continued failure to obtain NIH grants might cause the BBRI to not renew his appointment. I also told him that, if he could obtain "NIH or similar grants," that might allow us to reappoint him in two years [Ex. H].

13. BBRI allocates laboratory space based upon funding and utilization levels [Ex. C at p. B-06a]. Besides warning Vic that he might not be reappointed, my letter also reminded him of this policy [Ex. H]. Separate from Vic's academic appointment as a Senior Scientist, if he did not have funding, he was at risk of losing some or all of his laboratory space.

14. Vic appeared to me to realize the likelihood that he would be terminated and not reappointed. With no outside funding and his Bridge Support running out, he was under extreme pressure. Indeed, he appeared to be aggressively seeking funding, both to preserve his position and to obtain a salary to support himself.

15. The BBRI requires monthly Time and Effort Reports of all faculty members [Ex. C at p. A-06]. The reports show the percentage of time spent on each fund. Funds normally correspond to particular grants received by the faculty member. Vic's Bridge Support ended on September 15, 1997. At that time, Vic's Time and Effort reports switched from "Institutional Support" to "Grant Writing." As the Time and Effort Reports indicate, I believe Vic spent all his time preparing grants from the end of his Bridge Support on September 15, 1997, through December 31, 1997.

16. At some point, Vic obtained an SBIR grant. Such a grant is typically rather small and is of short duration. The BBRI did not generally desire such grants. Accordingly, I met with Vic to make sure he was aware that his short SBIR grant would not really help his chances of reappointment and that I would be bringing faculty candidates by to look at his laboratory space, indicating that it would be available for them [Ex. I].

17. The BBRI had some laboratory space in the basement, which was generally the least desired. Faculty members who were transitioning out of the BBRI were sometimes placed there temporarily. Indeed, the faculty member mentioned above whom the COR voted contingent bridge support was moved to that space before leaving the BBRI. I also informed Vic that we could make some space available for him in the basement [Ex. I].

I understand that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the above-identified patent.

Kathleen G Morgan — 3/7/07
Kathleen G. Morgan, Ph.D.

BOSTON BIOMEDICAL RESEARCH INSTITUTE
Program for the Future

STRATEGIC PLAN OUTLINE

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BOSTON BIOMEDICAL RESEARCH INSTITUTE
Program for the Future

STRATEGIC PLAN

SCIENTIFIC PROGRAM

I. Faculty Development

The long-range scientific strategy is to build upon our current reputation as the center for *muscle research* in the Boston community by not only further developing this area of investigation but also developing two additional interacting areas of research excellence. These two additional areas will be *cellular communication* and *cellular growth*. By developing strong basic science programs in these three overlapping specialties, we will have the necessary depth and scope to be able to make major contributions to health issues such as stroke, heart failure, and hypertension.

In the area of *muscle research*, additional scientists in the field of nonmuscle motility should be recruited. The successful recruitment of scientists working on novel molecular motors and on cytoskeletal-matrix interactions in nonmuscle cells will allow the Institute to apply its half-century of expertise in contractile proteins to much broader questions such as the "crawling" of cancer cells during metastasis and the trafficking of messages within cells. Thus, these scientists should be able to interact not only with the muscle group, but also the cell growth group and the cell communication group.

In the area of *cell communication*, the Institute already has considerable expertise in the area of transport proteins, and the recruitment of a channel person with patch clamp and perhaps channel cloning abilities would allow focused research on transmembrane communication in a much broader sense and in a manner that could greatly enhance investigations into motility and cell growth. Additionally, the recruitment of molecular biologists working on kinases and signalling cascades in both differentiated and proliferative smooth muscle cells would strengthen this focus group and assure interactions with the muscle and cell growth groups.

In the area of *cell growth*, the recruitment of a cell-cycle person or a growth factor person could greatly increase relevance of ongoing research into DNA and RNA replication mechanisms and would enhance the possible collaborative interactions of the muscle and cell communication groups.

A. New Faculty Recruitment

In the current era of financial crisis in biomedical research, fewer and fewer young graduates are entering basic research. This has created an intense competition among academic institutions for the best and brightest scientific graduates. At the same time, given the current shortage of federal funds for support of scientific

research, it is exceedingly difficult for the new scientist to become established as a recognized expert in a field of investigation and thus successfully compete for federal funds. Only the best of the young scientists do succeed and, on average, three to five years appears to be required for the new individual to become entirely self supporting. For this reason, the most competitive research centers are now offering five year packages of guaranteed support during the recruitment process. BBRI currently has the financial means to offer support for only two to three years, thus decreasing our competitiveness in recruiting new faculty and also, in some instances, forcing us to terminate promising young individuals before we have the opportunity to see any return on our initial investment. Supplementation of current resources by the creation of named Young Scientist Awards would greatly increase our chances of recruiting and retaining top investigators.

Estimated costs for recruiting two new Principal Investigators each year are: PI's salary $\$60K \times 2 = \$120K$; Tech $\$25K \times 2 = \$50K$; Salaries = $\$170K$; $\times 2.6$ indirects and fringes = $\$442K$; Start-up = $\$40K$; Supplies $\$10K \times 2 = 20K$; Relocation and remodeling = $\$30K$. Total: $\$532K$. Current estimates indicate that we should recruit two scientists per year in order to optimize grant income and maintain the vitality of the scientific programs.

B. Bridge Support

An equally urgent need is bridge funding of established investigators to cover the inevitable intervals when federal funding is delayed. A general goal will be to decrease the excessive dependence on NIH and similar sources for funding. Although federal funds will undoubtedly remain the main support for basic research, efforts should be made to create a "mixed portfolio" including industrial contracts, pharmaceutical and clinical collaborations, foundation support, and endowed, named Senior Scientist Awards. The interest on BBRI's endowment should be a major source for bridge funding, hence the importance of maintaining and increasing the current principal. Current experience indicates that providing bridge support for investigators averages $\$225,000$ annually.

We currently have the resources to provide support equal to the Principal Investigator's salary for one year. This policy inevitably results in loss of valuable intellectual capital. The long range goal is to develop resources to provide up to two years of support for the Principal Investigator and one member of the research team.

C. Fringe Funding

Currently, most of a Principal Investigator's time is focused on acquiring and maintaining NIH support. It is generally acknowledged that the NIH will only support ideas that are clearly documented to be entirely "feasible" by the presentation of considerable "preliminary data" and demonstrating that pilot studies have already been successfully performed. Truly novel and creative ideas cannot be supported by this mechanism and as a result the true potential of the

"intellectual capital" of the Institute is not being tapped. Hence there is a need for a funding mechanism to support ideas on the "fringe" of established concepts and pilot studies that will provide preliminary data that will eventually lead to NIH support. No funds are budgeted in this five-year period for this program, but fundraising efforts by the Development team could be focused on creating such a program.

D. Unreimbursed Indirect Costs

There are a number of agencies that provide grant funding that does not include indirect costs or, in other words, grants that do not reimburse the Institute for the cost of the entire project. Many of these grants, however, are highly prestigious and it is greatly to BBRI's advantage to have our faculty receive such awards. It is necessary, therefore, for BBRI to anticipate allocating funds to cover the unreimbursed indirect costs associated with these research projects. This currently involves the use of about \$150,000 of Institute funds annually for sharing incompletely reimbursed indirect costs.

E. Scientific Support Initiative

It is also imperative that BBRI initiate an outreach program to attract the necessary support resources for BBRI's scientists, e.g. students from local colleges and universities; post doctoral fellows; M.D.s in specialty training programs; visiting scientists; etc. BBRI offers a unique and ideal environment in which these talented young people can begin to explore or continue to build a career in basic research and our scientists will benefit from the additional research support as much as these individuals will benefit from the experience and the expertise at BBRI. It is equally important, however, that this initiative be implemented and maintained with minimal cost to the Institute.

II. Capital Equipment

A. Structural Biology Facility (attached)

B. Protein Expression Facility

Certain molecular biology techniques have now been sufficiently established to have become routine. In order to promote efficient utilization of BBRI resources and to capitalize on the collaborative nature of the Institute, efforts will be made to prevent the duplication of facilities that can be centralized and shared.

There is an immediate need for expression of proteins in essentially all BBRI laboratories. Rather than have each investigator independently devote personnel and time to a routine procedure, the Institute will set up a shared Protein Expression Facility. A Core Leader--a Principal Investigator-- will contribute 10% of his/her time to supervise the facility. A full-time research technician will be responsible for

day-to-day operations. Two-four large capacity incubators/shakers and two laminar flow hoods will be located in a small, self-contained laboratory. The core will be responsible for producing proteins primarily by using the baculovirus expression system, including keeping the virus stock, making the constructs, maintaining insect cell cultures, performing co-transfection and scaled-up production of proteins.

Funding for the core facility will be sought as part of the Smooth Muscle Program Project Grant (PPG), a competitive renewal grant to the NIH, and therefore will require minimal institutional funds.

III. Space

The current space available at BBRI allows the recruitment of only two additional investigators with rather modest space needs. Improving the air circulation and lighting in the basement and rearranging the existing space can optimize its use but, if the Institute is truly to be able to grow in the next millennium, some plan of action will have to be created for additional space.

BBRI still benefits from the lease negotiated with Schepens 25 years ago. In effect, BBRI does not pay for floor space itself but shares in the operating costs as outlined above. Operating costs are higher than those in a modern facility due to the inefficiencies inherent in an older facility. However, our per square foot cost of occupancy is considerably lower than at alternate sights.

The Institute has considered purchasing or leasing a different site for the facility. The lease does not allow BBRI to sublet space at Staniford Street, effectively limiting our sales market to Schepens Eye Research Institute. Although we know Schepens is seeking additional space, we feel it is unlikely that they will be prepared to offer us enough incentive to vacate. Economically, we can continue to enjoy the facility "rent free" for the next 25 years. It may be possible to renew the current lease but whether this would be a feasible, or desirable, option depends on the plans of the SERI, the condition of the building and the details of the new lease. Current strategic plans of the SERI appear to preclude extending the existing lease. It is to be recognized, however, that any plans to build onto the current building must be contingent on the eventual extension of the current lease.

Within the five-year Strategic Plan, we have factored in the following plans for the provision of adequate space.

Rental: Additional space could be rented in neighboring buildings. This could be done at a cost of \$25/sq. ft. in the Charles River Plaza or the building at 50 Staniford Street. For fiscal year 1997, we are considering renting 1,000 square feet and relocating the Accounting and Development offices to this space. The current Accounting Office area would then be renovated to accomodate the X-ray crytallography equipment and program staff.

For fiscal year 1998, two plans have been developed. The first would be in anticipation of the natural attrition in any organization and would focus on recruiting new faculty to use the space that would be vacated in the process of attrition. The second plan would be to rent additional space in the Charles River Plaza. Again, rental of this space would be \$25/square foot and it is likely we would be required to rent a minimum of 2,000 square feet initially, for a total of \$50,000 annually. Renovation of that space would require roughly \$120/sq. ft. If we assume a new investigator requires approximately 400 square feet, the initial construction cost for a laboratory would be \$50,000. The close proximity would allow for use of shared equipment and interaction with other faculty.

Looking ahead, beyond the five-year Strategic Plan, the decision remains to be made regarding relocation of the entire Institute.

Relocation: The entire Institute could relocate. This would be by far the most costly and time consuming option but should be considered an option for long term planning. Alternative laboratory space is available in other areas of the city. For example, laboratory space in the Longwood Medical Area rents for about \$55 per square foot (\$22,000 annually for a 400 square foot lab), with the advantage of proximity to Harvard University personnel and affiliates.

One specific concern is the fact that although the Institute has the academic prominence to host major international conferences, there is currently no on-site auditorium of the necessary size for such a venture. If funds could be obtained, a named conference center would significantly enhance the mission of the Institute to discover and disseminate new biological knowledge.

BUSINESS PROGRAM

The remarkable track record of success of the faculty in bringing in 90% of expenses from grants is a credit to their level of scientific excellence. At the present time, the Institute receives roughly 90% of its operating budget from these grants, the majority of which come from the NIH. Given the current shortage of funds at the NIH, allowing only 9-15% of meritorious grants to be funded, a major goal over the next decade will be to create a more "mixed" portfolio, which will reduce the Institute's dependence on faculty-initiated grants from the NIH and similar agencies and increase the supporting income from long and short term industrial contracts, foundation support, private donations, and return on BBRI investments to approximately 40% of the budget.

I. Revenues

A. Grants (Faculty-Initiated)

1. Federal

The U.S. government is the single largest supporter of biomedical research in the world; in 1994, the U.S. spent about \$33 billion for biomedical and related health research and development. The federal government provides approximately 80% of the monies spent each year for biomedical research at universities, medical schools, and not-for-profit research institutes. 87% of all federal support for biomedical research comes from funds allocated by Congress to the National Institutes of Health (NIH); the 1995 NIH budget was \$11.3 billion.

The NIH continues to be BBRI's major source of grant funding. Occasionally, the Insitutute also obtains funding from the National Science Foundation (NSF). The typical Individual Investigator Initiated Research Project Grant, termed RO1, provides BBRI with direct research costs (salaries, research supplies, etc.) and indirect costs (i.e. those costs incurred by BBRI such as light, heat, administrative services, etc.).

The grant process at NIH is a long, stressful process for the scientist who has submitted a grant. The NIH receives grant applications 3 times a year. The applications are generally 30-50 page documents and require that all proposed experiments be accompanied by preliminary experiments to certify feasibility. Approximately 3-4 months after receipt, the grants are subjected to "peer review" by one of several "Study Sections", i.e. a committee of scientists from across the country that meets in Bethesda, MD. for 2-3 days to construct a relative ranking of the grants by merit. Currently, 4 of our faculty members serve on NIH Study Sections as nationally recognized experts in their fields.

The study section assigns a "priority score" from 1.00 to 5.00 to each grant—with 1.00 being most meritorious and 5.00 being least meritorious. Recently, in an effort to decrease administrative cost and time, a "triage" process has been implemented and grants that are evaluated to be in the worse half (generally scores of 2.5 and larger) do not receive full review by the committee or a score.

When the study section completes its evaluations, the scores are "percentiled" against past scores recommended by that individual study section. Only percentiles are compared between study sections, in order to normalize for differences in the generosity or toughness of scientists on the individual study sections.

Three to four months after the study sections complete their work, the grants receive a second level of review by the Councils of the NIH. Each Council will set a "payline". Current paylines are ranging from 9-15%. Often a grant is borderline and, also because of political uncertainties, the Principal Investigator may not know for sure whether he or she is funded until shortly before the start date of the grant, 3-4 months after Council meets. Thus there is significant lag (generally 9 months) between submission and funding of successful grants.

Because of the shortage of funding for excellent grants, most investigators expect to need to revise their applications at least once, adding another 9 months to the delay in funding. Current efforts are being made to try to submit renewal applications for funding one year early in an effort to keep programs (and personnel) continuous.

2. Other Agencies (Non-Federal)

There are several private national foundations to which investigators can apply for support. However, these sources require that the research be disease-oriented. Also, these grants are relatively small in dollar amount, and they do not provide continuous support of ongoing investigations. These smaller grants can be very useful, however, in adding needed personnel to a project or in providing support of an ongoing project while waiting for NIH funding to be awarded.

The Institute has received, and continues to receive, generous support from the Muscular Dystrophy Association for its work on muscle disease, from the American Heart Association for its work on stroke, heart failure and hypertension, and from the American Cancer Association for its work on mechanisms of cell growth.

3. Pharmaceutical/Industrial Collaborations

Increasing the revenue from industrial collaborations is a longterm goal; therefore, revenues from this initiative are not included in the five-year Strategic Plan. A task force should be established to acquire information on companies that may have long range goals or specific ongoing programs that mesh well with the goals and expertise of the Institute. This group should plan the initiation of contacts with the appropriate companies. The goals will be: (1) to initiate an "intimate relationship" with 1 or 2 major pharmaceutical firms, allowing them to have a "window" on evolving, state of the art, basic science in return for licensing rights; (2) to initiate individual scientific collaboration between Industry and the Institute that may result in sponsored research; (3) to obtain named sponsorship for seminar programs; (4) to establish Sabbatical/Internship Programs that will allow industrial scientists and Institute scientists to learn specialized technologies and perform collaborative studies.

A joint venture with the Beth Israel Hospital has led to the establishment of the Boston Collaborative Heart Failure Center, encompassing a number of specific collaborative "discovery" research projects aimed at the cure of heart failure, through patient testing and multi-center clinical trial coordination of new potential therapies and diagnostic tools. Significant corporate support for the Center is being actively recruited.

Long term contracts with pharmaceutical companies may be of considerable benefit in providing financial stability, intellectual input, and access to new experimental tools. However, because of concerns regarding academic freedom, co-existing NIH

regulations, and legal complications, considerable caution should be applied before entering into such ventures.

B. Development/Public Relations

There are basically 3 sources of revenue for charitable contributions to BBRI:

REVENUE SOURCES

Individuals
Foundations
Corporations

Programs need to be strengthened in individual and foundation giving, and the need to develop and implement a strategy of fundraising from corporations should be evaluated and moved forward. It is of critical importance that the fundraising programs related to these revenue sources be built up and strengthened so as to provide BBRI with a solid and consistent Annual Fund program.

The revenue goals, however, should also be placed within the reality of the "marketplace", i.e. should be comparable to those of other basic research organizations somewhat similar to BBRI, e.g. Worcester Foundation or Jackson Labs. The fundraising revenue goals for BBRI should be realistic and therefore achievable, so as to create a sense of accomplishment and confidence among the solicitors and donors. One way of reaching this objective is to focus the Annual Fund on projects or programs, with clearly defined goals in each area. Following are suggestions for giving programs.

GIVING PROGRAMS

INDIVIDUALS

Board
Direct Mail
Special Events
Planned Giving
Major Gifts

The most significant addition to the current individual giving program is the development and implementation of a major gifts or special gifts program. Initially we will identify 5-10 major gift prospects and, with the assistance of volunteers, begin cultivating them for a major gift to BBRI. As we now have the Peabody Challenge in place, the major giving program will be focused on raising the \$300,000 needed to meet the challenge and purchase the X-ray crystallography equipment.

CORPORATE

We are beginning to move forward with two facets of a corporate giving program: soliciting new corporate donors for BBRI through proposals (Boehringer Mannheim; Boston Scientific), and assessing the need for and development of a volunteer Corporate Committee.

FOUNDATIONS

We have, in the past, benefited from the generous support of local foundations. We should strive to maintain this support, while broadening our contacts to national foundations. The possibility of programmatic or individual support from national foundations such as the Howard Hughes Medical Institute, Kresge Foundation, Keck Foundation, etc., is underway and it is anticipated that several proposals will go to national foundations in the second half of the year. These foundations may be appropriate sources for major items of capital equipment to complement new programs or recruitments.

Looking forward to the long term Development focus, two needs of the Institute emerge that will require vigorous fundraising activity: increasing BBRI's endowment, and building new space for the Institute. As these cannot happen concurrently, strategic decisions need to be made as to the priority for future campaigns; however, it is essential that both are undertaken at some time in the future.

PUBLIC RELATIONS

Lack of communication with the general public appears to be a major impediment to soliciting charitable contributions to BBRI, and effort should be invested in improving the visibility of the work done at the Institute while making the importance of this work more understandable. Recognition of the longterm importance and value of investment in basic science requires considerable vision and sophistication on the part of BBRI supporters, and this challenge needs to be considered as the public relations activity moves forward. The focus of the Institute has been sharpened and the mission clarified without sacrificing the fundamental commitment to basic research; these objectives must be continued and strengthened. With the assistance of a public relations consultant, a solid, comprehensive foundation for increasing and improving BBRI's public relations efforts will be built and implemented. The three areas that the public relations activity will focus on strengthening and expanding are: 1) media relations; 2) communications/publications; and 3) government (federal, state, and local) liaison development.

Additionally, the visibility of the Institute can be raised by building bridges with the Harvard teaching hospitals and other area institutions, and by sponsoring high

quality symposia. With respect to clinical interactions, a work group is needed to outline the possibilities for interaction with clinical departments at Harvard hospitals. The combined expertise and interests could form the basis for a number of individual, high visibility collaborations as well as potential SCOR and Center grant applications. At the present time, opportunities appear to be greatest with regard to interactions with the Department of Medicine at the Beth Israel Hospital in Boston, where the new Director of the BBRI will continue to hold a Faculty position; however, possible collaborations with all Boston hospitals will be explored and considered.

Three specific initiatives will be considered: (1) An application for an NIH-funded training program to allow research-oriented clinical trainees at Boston-area hospitals to pursue 2-3 years of basic research training at the Institute. The cross-fertilization of expertise should be of interest to all parties involved; (2) the creation of a foundation (similar to Whitaker) to fund interactive projects between Boston-area hospitals and BBRI; members of both institution's governing boards will be invited to contribute, and peer review of grant applications will be performed by four individuals from the two institutions; (3) the Boston Collaborative Heart Failure Center.

In regards to symposia, an international symposium honoring the career of John Gergely will be held on July 27-29, 1996, and a second "Seidel Symposium" in the spring of 1997, continuing with a focus in the area of Muscle will be organized within the next two years and should become a regular event. Consideration should be given as to whether the focus should continue to be smooth muscle. Additionally, the idea of an event possibly co-sponsored by another research institute and the BBRI, possibly funded by a private foundation or covered by public broadcasting to investigate the future of basic biomedical research should be developed and, at the appropriate time, a work group should be formed to implement the project.

The BBRI public relations plan is composed of several strategies, each aimed at a very specific objective for the coming year. The foundation that should result from the development and implementation of these concurrent pieces will, hopefully, provide the base on which to continue to build in the future.

C. Investments

BBRI, through the collective efforts of its faculty and Development Office, has built up an investment portfolio of over \$7,000,000. The portfolio is managed by the Investment Committee, comprised of Trustees and senior management staff of the Institute.

The Investment Committee has established a set of investment goals within defined parameters. Currently, the portfolio consists of mutual funds ranging from money market to aggressive growth funds. Historically, 5% of the average portfolio balance for the prior three years is available for annual operations. In addition, it is

anticipated that, over the long run, investment income will be sufficient to pace the principal growth with inflation.

D. Technology Transfer

Since 1982, BBRI scientists initiated a number of projects that were funded by corporate research contracts, with the three major contracts bringing \$1.6 million in research funds to BBRI in the period 1982-1994. In addition, through the auspices of BBC, a solely-owned for-profit subsidiary of BBRI, Institute scientists have been awarded five phase I grants through NIH's Small Business Innovative Research (SBIR) program. Eight patents have been issued to BBRI, and one of these is just about to produce an income for BBRI from a licensing agreement.

No matter how impressive this record may be for an institute as small as BBRI, it was the result of sporadic initiatives by individual scientists and not the result of long-term planning. There is no question that a systematic technology transfer effort could have opened additional opportunities for corporate research and licensing agreements. In recognition of this important potential source of research funding and revenue, BBRI has recently become a member of the United Office of Technology Transfer of MBRI (Massachusetts Biotechnology Research Institute), which provides effective technology transfer services to a number of Boston area academic institutions.

In the past year, MBRI has conducted a detailed technology assessment of BBRI and has played an important educational role by increasing the awareness of BBRI scientists of technology transfer opportunities. This has set the stage for a systematic technology transfer effort, whose core will be the marketing of BBRI intellectual property to biotechnology companies, major pharmaceutical companies, and venture capital. An important component of this initiative will be to identify technology areas in which BBRI has particular strengths and market those as a package so as to enhance their impact and visibility. Another opportunity is offered by the SBIR funding mechanism, especially through the large phase II grants, which would require a reexamination of the role of BBC, including the possibility of joint ventures between BBC and established biotechnology companies. It is hoped that through aggressive efforts along these lines, research funding and licensing income from corporate sources will expand significantly above the current \$100,000 annual average.

III. Expenses

A. Directs

The responsibility of budgeting for and monitoring the expenditure of direct costs associated with a specific grant has traditionally been held by the Principal Investigator who submitted the grant. Such costs include salaries and fringe benefits, supplies, publication and travel related to a grant. BBRI has always maintained a

policy of conserving research funds and has been very successful, thanks to the efforts of the faculty, in limiting unnecessary spending of grant-related revenue.

This system of allocating and monitoring grant-related revenue is in keeping with BBRI's overall philosophy of encouraging independence and creativity among the faculty, and we feel strongly that this policy is a valuable incentive in the recruiting process.

B. Indirects

The Institute has been, and continues to be committed to keeping its administrative staffing levels lean and multi-functioning. In many cases this means foregoing individuals hired specifically to perform functions such as purchasing, research administration and equipment maintenance and scheduling. Instead, systems are designed in such a manner to provide these functions with existing personnel, e.g. the Director acts as both Chief Executive Officer while managing a full time laboratory; the Assistant Director is responsible for all physical plant management as well as financial matters; Principal Investigators assume the purchasing role as well as pursuing and expanding their research projects.

The indirect cost rate will be negotiated in early 1997 and will take effect September 1, 1997. This is an area of critical concern to the Institute. There is a clear justification for an increase of the indirect cost rate. However, the Department of Health and Human Services is under pressure to lower indirect cost rates. We have made an assumption in the budget that our indirect cost rate will be increase by 10% of its current rate (to approximately 96% of personnel costs).

Although we have hit a particularly trying time for annual funding, we have a solid financial base, are debt-free, and have a commitment of financial and managerial support from the Board of Trustees. We believe the influx of new talent, combined with the scientific goals established in this plan, will be the foundation for our continued success.

NEW ISSUE

In the opinion of Ropes & Gray, Bond Counsel to the Institution, under existing law, interest on the Series 1999 Bonds is excluded from the gross income of the owners of the Series 1999 Bonds for federal income tax purposes, assuming continued compliance by the Issuer and the Institution with the Internal Revenue Code of 1986, as amended. Interest on the Series 1999 Bonds is not an item of tax preference for purposes of the federal alternative minimum tax imposed on individuals and corporations. However, interest on the Series 1999 Bonds will be taken into account in determining adjusted current earnings for the purpose of computing the alternative minimum tax imposed on certain corporations (as defined for federal tax purposes). In the opinion of Bond Counsel to the Institution, under existing law, the Series 1999 Bonds and any income derived therefrom, including any income from any sale, exchange or transfer of the Series 1999 Bonds, shall at all times be free from Massachusetts taxation, although the Series 1999 Bonds and the interest thereon are included in the measure of Massachusetts estate and inheritance taxes and of applicable Massachusetts corporation excise and franchise taxes. For federal and Massachusetts tax purposes, interest includes original issue discount. See "TAX EXEMPTION" herein.

\$17,000,000

MASSACHUSETTS DEVELOPMENT FINANCE AGENCY

Revenue Bonds

(Boston Biomedical Research Institute, Inc. Issue - Series 1999)

Dated: February 1, 1999

Due: February 1, as shown below

The Massachusetts Development Finance Agency Revenue Bonds (Boston Biomedical Research Institute, Inc. Issue - Series 1999) (the "Series 1999 Bonds") are issuable only as fully registered bonds without coupons and, when issued, will be registered in the name of Cede & Co., as Bondowner and nominee for The Depository Trust Company ("DTC"), New York, New York. DTC or its custodial agent will act as securities depository for the Series 1999 Bonds. Purchases of the Series 1999 Bonds will be made in book-entry form, in the denomination of \$5,000 each or any integral multiple thereof. Purchasers will not receive certificates representing their interest in Series 1999 Bonds purchased. So long as Cede & Co. is the Bondowner, as nominee of DTC, references herein to the Bondowners or registered owners shall mean Cede & Co., and shall not mean the Beneficial Owners (as hereinafter defined) of the Series 1999 Bonds.

Principal and semiannual interest on the Series 1999 Bonds will be paid by State Street Bank and Trust Company, as trustee (the "Trustee") and paying agent. So long as DTC or its nominee, Cede & Co., is the Bondowner, such payment will be made directly to DTC. Disbursement of such payments to the DTC Participants is the responsibility of DTC and disbursements of such payments to the Beneficial Owners is the responsibility of the DTC Participants, all as more fully described herein. Interest will be payable on August 1, 1999 and semiannually thereafter on February 1 and August 1 to the Bondowners of record as of the close of business on the fifteenth day of the month preceding such interest payment date.

The Series 1999 Bonds shall be special obligations of the Massachusetts Development Finance Agency (the "Issuer") doing business as "Mass Development".



MASSDEVELOPMENT

The Series 1999 Bonds will be issued pursuant to a Loan and Trust Agreement dated as of February 1, 1999 (the "Agreement") among the Issuer, Boston Biomedical Research Institute, Inc., (the "Institution") and the Trustee. The Issuer will loan the proceeds of the Series 1999 Bonds to the Institution. The Series 1999 Bonds are payable solely from and secured by payments to be made to the Trustee for the account of the Issuer by the Institution and from such other funds as may be available therefor under the Agreement. Reference is hereby made to this Official Statement for pertinent security provisions of the Series 1999 Bonds.

THE SERIES 1999 BONDS DO NOT CONSTITUTE A GENERAL OBLIGATION OF THE ISSUER OR A DEBT OR PLEDGE OF THE FAITH AND CREDIT OF THE ISSUER OR A DEBT OR PLEDGE OF THE FAITH AND CREDIT OF THE COMMONWEALTH OF MASSACHUSETTS OR ANY POLITICAL SUBDIVISION THEREOF; EXCEPT TO THE EXTENT PAID FROM BOND PROCEEDS, THE PRINCIPAL OF, PREMIUM, IF ANY, AND INTEREST ON THE SERIES 1999 BONDS ARE PAYABLE SOLELY FROM THE REVENUES AND FUNDS PLEDGED FOR THEIR PAYMENT IN ACCORDANCE WITH THE AGREEMENT. THE ISSUER HAS NO TAXING POWER.

MATURITIES, AMOUNTS, RATES, AND PRICES OR YIELDS

Due February 1	Principal Amount	Interest Rate	Price or Yield	Due February 1	Principal Amount	Interest Rate	Price or Yield
2001	\$255,000	5.00%	4.25%	2006	\$330,000	5.00%	4.85%
2002	270,000	5.00	4.45	2007	345,000	5.00	4.95
2003	285,000	5.00	4.60	2008	360,000	5.00	100
2004	295,000	5.00	4.70	2009	380,000	5.10	100
2005	310,000	5.00	4.75				

\$5,170,000 5.65% Term Bonds Due February 1, 2019 to yield 5.68%

\$9,000,000 5.75% Term Bonds Due February 1, 2029 - Price 100%

(Accrued interest to be added from February 1, 1999)

THE SERIES 1999 BONDS ARE SUBJECT TO REDEMPTION PRIOR TO MATURITY AT VARIOUS PREMIUMS, OR AT PAR UNDER CERTAIN CIRCUMSTANCES, AS MORE FULLY SET FORTH HEREIN.

The Series 1999 Bonds will be offered, when, as and if issued and accepted by the Underwriter, subject to prior sale, to withdrawal or modification of the offer without notice, and opinions as to legality and certain other matters by Ropes & Gray, Boston, Massachusetts, Bond Counsel to the Institution. Certain legal matters will be passed upon for the Institution by its counsel, Ropes & Gray, Boston, Massachusetts. Certain legal matters will be passed upon for the Underwriter by its counsel, Edwards & Angell, LLP, Boston, Massachusetts. The Series 1999 Bonds are expected to be available for delivery to DTC in New York, New York, or its custodial agent, on or about February 19, 1999.

State Street Bank and Trust Company

February 11, 1999

rates on NIH applications versus that of the average for all AIRI members for fiscal years 1993 through 1997 (the last year for which complete data is available).

BBRI's Success Rates on NIH Applications vs. AIRI

	Number of Applications			Number of Grants Awarded			Success Rate		
	Higher			Higher			Higher		
	AIRI	Ed	BBRI	AIRI	Ed	BBRI	AIRI	Ed	BBRI
1993	929	17,097	9	258	3,993	3	27.8%	23.4%	33.3%
1994	973	18,405	8	298	4,554	2	30.6%	24.7%	25.0%
1995	1,041	18,159	9	327	4,818	0	31.4%	26.5%	0.0%
1996	963	16,915	18	327	4,602	7	34.0%	27.2%	38.9%
1997	949	16,541	19	330	5,015	4	34.8%	30.3%	21.1%

Source: NIH

Success rates for grant applications from all types of institutions have historically ranged from 23% to 34%. In general, AIRI members have obtained higher success rates for its grant applications than institutions of higher education. As shown in the above table, BBRI's success rate for new grant applications over the past five years has varied from 21% to 39%, excluding the year of 1995. BBRI did not have any of its NIH grant applications approved in fiscal year 1995. In fiscal year 1995, the Board appointed the current Director to manage the Institute. Of the nine applications submitted that year non-performing principal investigators made five applications in hopes of gaining funding before being subject to any new grant application rules of the Director. All of these investigators have subsequently left the Institute due to their lack of ongoing grant support. One principal investigator submitted two applications that, after a revision, were later funded by the NIH. Currently this investigator holds three NIH grants. Another investigator under Merit Award Status, the most prized grant funding, had funding delayed until the following year when the second half of the ten-year merit award was issued for \$2.2 million. Finally, one application simply did not receive funding from NIH. This principal investigator has subsequently received two Small Business Innovative Research ("SBIR") grants.

Patents and Technology Transfer

The passage of Public Law 96-517, the Bayh-Dole Act, in 1980 permits BBRI and all NIH grantees to retain title to and manage the commercialization of intellectual property generated with NIH funding. Under the Bayh-Dole Act, the federal government has a right to take over the licensing effort with respect to a given invention in the event that BBRI is not diligent in its licensing efforts. To date, the federal government has not exercised this right. While BBRI has been successful in its licensing efforts to date, there is no certainty that such efforts will be successful in the future.

In 1982, BBRI established the Boston Biotechnology Corporation ("BBC"), a solely-owned for-profit subsidiary. As a result of the formation of BBC, BBRI has entered into research funding agreements with for-profit pharmaceutical and biotechnology firms that have provided funding in exchange for technology licenses and/or options to license BBRI technology on various terms and conditions. The agreements have helped generate unrestricted funds and support for specific research projects and provided a vehicle to transfer BBRI's basic research findings into commercial projects. In 1993, BBRI retained Medtech Capital, Inc. (formerly known as LifeTech Capital, Inc.) to assess technologies at BBRI and initiate marketing efforts. In 1995, BBRI became a member of the Unified Office of Technology Transfer of the Massachusetts Biotechnology Initiatives. To assist in these activities and assure compliance with government regulations, BBRI established its Patents and Technology Transfer Committee in 1995. Since 1982, BBC has sponsored six successful applications for SBIR grants for research that was done using BBRI facilities. Currently BBC holds one active SBIR grant.

Management's Discussion of Recent Financial Performance

Operations. The Institute has achieved operating gains and an excess of total unrestricted support over expenses in 27 of the last 29 years. The following table shows the operating performance and return on operating revenue for BBRI over the past five years.

Operating Performance

	1994	1995	1996	1997	1998
Increase (decrease) in unrestricted net assets	\$539,168	\$732,669	(\$643,726)	\$1,687,936	\$822,007
Unrestricted support	\$7,207,143	\$7,446,777	\$6,092,687	\$6,850,537	\$7,745,907
Operating Margin	7.5%	9.8%	(10.6%)	24.6%	10.6%

Approximately 90% of BBRI's grant revenue generates from funding by the NIH. Revenues from grants and contracts has decreased from a peak of \$6,956,725 in 1994 to \$5,164,438 in 1998. The lower level of grant revenues in year 1997 and 1998 is a result of the slowdown in new grant applications and approvals that occurred in 1995 during the appointment of the new Director. Management also attributes this decline to the combination of recruitment time of new scientists coupled with the NIH's lengthy grant application and approval process. All grants issued by the NIH are awarded after an intensive competitive grant application process. Assuming approval, the grant is funded nine months from the application date. In addition, in 1995, BBRI developed a strategic recruitment plan to hire two new principal investigators per year. This recruitment plan coincided with the expiration of several grants and the appointment of the new Director.

Management anticipated the decline in grant revenues in 1996 and 1997, and opted to position itself for future expansion. BBRI let go several investigators that did not have grant funding and started a new recruitment program. BBRI successfully recruited two new investigators in August and September 1995, and supported their research activities until they received grant funding in May and March, 1996, respectively. In addition BBRI retained several investigators whose grant funding was interrupted but whom BBRI felt were likely to regain funding. This strategic decision led to an operating loss in 1996, but management believes it has strengthened the Institute moving forward.

Since 1996, BBRI has recruited six additional investigators, three of whom have received funding, two of whom are awaiting decisions on grant applications, and the remaining investigator joined the BBRI faculty in the January, 1999. In 1997, BBRI moved several of its investigators into non-salaried positions reflecting their grant funding status.

For the five month period ending November 30, 1998 compared with five months ending November 30, 1997, grant revenue increased 6.9% while salaries and benefits only increased 6.0%. During the same period, BBRI experienced an investment income loss of \$102,912. This loss is primarily related to a downturn in the stock market during this period and consists of \$340,770 of unrealized losses and \$237,858 of realized gains, dividends and interest. During this five month period, BBRI received eight new grant awards. Four of these grants are expected to increase BBRI's revenue in the second half of 1999.

The NIH grants range from three to five years with the targeted goal of NIH to have the average grant length of four years. This grant length provides stability for the Institute and creates a revenue backlog. The current backlog of grants approved for funding for the Institute was \$17.5 million (as of June 30, 1998) and is expected to increase. Since June 30, 1998 the Institute has received eight additional new grants approved totaling \$5,607,337. Management fully anticipates grant revenue to return to and exceed 1994 results by the year 2000. The 1999 budget projects an increase in grant revenues of 20% to \$6.27 million.

Appendix A

The October 1995 revision to OMB Circular A-122 went into effect on September 29, 1995. This revision allows interest expense to be recoverable from federal sources. Before the passage of this revision, most research institutes leased facilities rather than financed the purchase of the facility with debt because only lease expenses were subject to indirect cost recovery. Due to the change in these interest recovery regulations, interest is now an allowable cost recovery item on capital expansion. Management has alerted the Department of Human and Health Services as to its plans to issue debt to fund the new laboratory facility and expects to pass on a significant portion of the new debt service when the Institute's new negotiated direct cost recovery rate goes into effect on July 1, 1999.

Balance Sheet. Management has placed an ongoing emphasis on liquidity and cash flow. The following table depicts the Institute's unrestricted cash and investments, operating expenses (less depreciation and amortization), and days cash on hand for the last five fiscal years. Days cash on hand is calculated by multiplying the Institute's unrestricted cash and investments by 365 (days/year) and dividing the results by total operating expenses less depreciation and amortization expenses.

Unrestricted Cash and Investments (Market Value)

	1994	1995	1996	1997*	1998
Unrestricted Cash and Investments	\$6,596,153	\$7,503,434	\$7,086,419	\$7,701,747	\$8,376,795
Operating Expenses (less depreciation & amortization)	\$6,479,642	\$6,545,906	\$6,529,901	\$4,993,143	\$6,608,281
Days Cash on Hand	371.6	418.4	396.1	469.2	462.7

* Ten months of operating expenses calculated from August 31 to June 30 (303 days)

The Institute's unrestricted cash and investments increased from \$6,596,153 in 1994 to \$8,376,795 in 1998, an increase of 27%. In 1996, days cash on hand decreased from 418.4 to 396.1 due to a \$780,000 decrease in cash reserves. This is primarily due to the Institute's recruiting strategy which required the Institute to support two new investigators until they received grant funding. As of June 30, 1998, less than \$500,000 of the Institute's \$8.8 million of investments are permanently restricted.

Similarly, total net assets of the Institute has grown significantly, increasing from \$8 million in 1994 to approximately \$11 million as of June 30, 1998. Management attributes this growth to investment appreciation and a growing fundraising program.

Budget Procedures and Financial Controls

The Chief Operating Financial Officer meets with the Institute's scientists to draft a budget proposal for the following fiscal year. The Budget and Finance Committee reviews the budget in detail before submitting it for approval by the full Board. The Board sets the directives for the budget. At the June Board meeting, the final proposal for the following year is submitted for Board approval. Management reviews budget and expenditures each month and reports any variance to the Budget and Finance Committee.

Investments

As of January 15, 1999 BBRI had total investments of \$8,495,289, at market value, of which \$7,696,666 is unrestricted, \$335,574 is temporarily restricted and the remainder is restricted. Currently, the investment portfolio is invested in mutual funds with an allocation of approximately 80% equities and 20% fixed income.

the lead investigator. This grant accounts for approximately 25% of BBRI's grants and contracts revenue. In December of 1997, this grant was renewed until November, 2002.

The following table summarizes investigators additions and deletions of salaried scientists during the fiscal years ended August 31, 1995 through June 30, 1998. Salaried scientists that became non-salaried staff in the subsequent fiscal year are counted as deletions to the employed scientific staff. In addition, non-salaried scientists that became salaried employees in the ensuing year are counted as additions to the employed scientific staff.

**BBRI's Historical Number of Salaried
Investigators**

<u>Investigator</u>	<u>1995</u>	<u>1996</u>	<u>1997</u>	<u>1998</u>
Additions	1	3	2	4
Deletions	0	4	2	4

Many of BBRI's scientists have been honored by national and international scientific communities for their achievement including:

- BBRI has received two NIH Merit Awards. Merit awards are provided, in limited numbers, to selected investigators who have demonstrated superior competence and outstanding research. These awards provide the opportunity to extend a previously approved grant for an additional five years beyond the original period of the grant.
- BBRI faculty are consistently called upon to serve on NIH Peer Review Panels, scientific advisory boards and editorial boards for scientific publications.

BBRI scientists publish approximately 30 to 40 articles in scientific journals annually.

Employees

As of June 30, 1998, BBRI had 75 full-time equivalent employees. BBRI offers a competitive benefits package to full-time employees including retirement, life, medical, disability and dental insurance. Employees may invest in a tax-deferred retirement account with TIAA/CREF. In addition, employees are eligible for tuition reimbursement up to \$3,500 per academic year for work related courses and their children are eligible for tuition remission.

None of the Institute's employees is represented by a collective bargaining unit and no union or union organization is in place or contemplated to Management's knowledge. BBRI considers its relationship with its employees to be excellent.

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BOSTON BIOMEDICAL RESEARCH INSTITUTE

POLICIES AND PROCEDURES MANUAL

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 - F. Immigration
 - G. Institutional Policies
 - H. Miscellaneous
 - I. Travel
 - J. By-Laws and Operating Guidelines
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TIME AND EFFORT REPORTING

Time and effort reporting is done on a pre-prepared listing which is distributed monthly by the Accounting Office.

There will be a page for each fund number showing the employees charged to the fund and the percentage of their salaries. This listing must be signed and dated by the Principal Investigator and returned to the Accounting Office.

Transfers, if required, will be posted to these sheets by the Accounting Office from signed Authorization for Transfer of Expenditure forms.

SICK AND VACATION TIME REPORTING

Support staff sick and vacation time is reported on a monthly basis. The Sick and Vacation Leave form is distributed by the administrative assistant. The completed form must be signed by the staff member and approved by the Principal Investigator, then returned to Accounting for centralized payroll record keeping.

FACULTY REAPPOINTMENT

Any Scientist, Principal Scientist, or Senior Scientist shall be notified one year before the term of his/her appointment expires whether the appointment will be recommended for renewal by the Committee on Research. Scientists who have received formal warnings that they may not be reappointed may be granted one-year extensions. The decision whether to give an extension will be made in a timely manner. If no formal warning is given, scientists are eligible for full term reappointments.

Amongst the criteria for considering reappointments are:

- Continued scientific productivity as evidenced by publications and grants.
- Service to the Institute.
- Scientific reputation.

Any Scientist, Principal Scientist, or Senior Scientist appointment not recommended for renewal shall be extended so as to provide one-half, one, or two years respectively, between the action and the expiration of the current appointment.

JOB DESCRIPTION

SCIENTIST

Scientists are appointed for three-year terms, Principal Scientists for four-year terms and Senior Scientists for five-year terms. These ranks correspond to the positions of Assistant Professor, Associate Professor, and Full Professor, respectively. Persons appointed to this category are classified as regular employees and may be on a full-time or part-time basis.

Qualifications:

The qualifications for an appointment are as follows:

Senior Scientist: established scientists of high standing internationally in their field as evidenced by at least two letters of recommendation by renowned colleagues.

Principal Scientist: should have repeatedly demonstrated the ability to compete successfully as a Principal Investigator for a research grant or equivalent productivity at the national level.

Scientist: usually has had at least three years of post-doctoral or equivalent experience prior to the appointment and is usually the Principal Investigator of a research project.

GRANTS

BRIDGE SUPPORT FOR FACULTY

FIRST YEAR

- A first year of bridge support in an amount equal to the PI's salary is given to productive members of the faculty contingent upon timely submission of competitive grant applications.
- The amount of bridge support is proportional to the percentage of the PI's time allocated to the specific grant whose funding is delayed.
- If funding is received before bridge support runs out, unused moneys will be returned to the Institute.
- Application does not require submission of pink sheets and scores but does require a financial statement.
- For faculty members who have previously received bridge support, a new round of bridge support can only be obtained after successfully obtaining a full R01-type grant (e.g. NIH, NSF, SBIR) of three years or longer, or comparable supports.

SECOND YEAR

- Only available in exceptional circumstances, provided the Board of Trustees approves the request.
- PI must submit to the COR with the application for a second year of support:
 - Scores and pink sheets from most recent NIH review
 - CV
 - Letter outlining the PI's plan for successfully building his/her program and obtaining funding
- Criteria to be used in making decision of whether to recommend second year of bridge support:
 - Probability of funding
 - Excellence of science
 - Contributions to Institute
 - Programmatic fit

Boston Biomedical Research Institute



ANNUAL REPORT

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MESSAGE FROM THE PRESIDENT

One consideration in formulating our five-year Strategic Plan was the notion of critical mass. To achieve our goal of maintaining BBRI's leadership position in our biomedical research field required expansion of the scope of our muscle research and adding complementary research areas. Dr. Kathleen Morgan, BBRI's Director will summarize the excellent progress in this regard.

To further strengthen the research programs, significant additions to the scientific staff are required. Our ongoing recruitment program has been extremely successful in attracting dedicated, promising young scientists. However, new scientists and new equipment lead to pressures on our laboratory facilities, which we share with our landlord, Schepens Eye Research Institute (SERI).

The Schepens Eye Research Institute has also undertaken expansion that has necessitated leasing space in the surrounding neighborhood. During the latter part of fiscal year 1998, BBRI and SERI have explored various options for satisfying our

mutual need for space. We anticipate in Fiscal Year 1999 adopting a facilities plan consistent with BBRI's vision of its future programs.

Hand-in-hand with assembling a critical mass of faculty and research programs is the need to expand the circle of BBRI friends whose generous gifts provide the seed money for these efforts. While our successes to date significantly increased our grant base, grants do not cover the costs of supporting new scientists, equipping laboratories or providing bridge support for experienced scientists.

1998 was a very successful year for BBRI and I thank all our loyal donors for their support. 1999 promises to be another tremendous

and challenging year - one which should be invigorating for us all. It will provide a superb opportunity to introduce the exciting world of biomedical science to a new group of friends. What could be more rewarding than being a part of an organization which has and will continue to have a beneficial impact on the health of this generation and that of our children and grandchildren.

"1998 was a very successful year for BBRI and I thank all our loyal donors for their support. 1999 promises to be another tremendous and challenging year - one which should be invigorating for us all."



David A. Gibbs, Sc.D.

MESSAGE FROM THE DIRECTOR



This has been an exceptionally active and satisfying year at the Institute. We are three years into the five-year Strategic Plan for the Institute that was put together at my arrival at the Institute and it is a delight to see how much of that plan the faculty and friends of the BBRI have accomplished. In this short time we have: significantly increased our grant base, added eight new members to our faculty, had a record breaking fundraising campaign to purchase state of the art crystallography equipment, increased the number of collaborations with researchers in area hospitals, and, most importantly, we have "pushed back the frontiers of our knowledge" in areas relevant to heart disease, stroke, Alzheimer's and cancer! You will find some of those stories in this Annual Report.

As our supporters know, the fundamental science at the Institute has always been strong in the field of muscle research. As part of the Strategic Plan, we have significantly expanded the scope of our muscle research and have strengthened our research in two new, but intentionally overlapping areas, signaling (or cell communication) and regulation of cell growth. Indeed the continued success of our research programs and our plans to expand them has lead us into negotiations with our landlord and neighbor, the Schepens Eye Research Institute. Both institutes require more research space and we are looking closely at what will be most beneficial and appropriate to the future plans of BBRI.

The scientists featured in this Annual Report work at the intersection of BBRI's three main research areas. Dr. Coluccio is an expert in the field of non-muscle motility – a term that may seem to be a bit of an oxymoron at first glance – but in reality, it is a hot new field of muscle research. Work in this field has resulted in the discovery that the same sort of "molecular motors" that allow our arms and legs to move also control processes as diverse as the metastasis of cancer cells and the directional growth of neurons in a baby's brain.

Dr. Toker works primarily in the field of signaling, but as you will read, in the process of trying to figure out

how the cell signals are communicated – and move from one molecule to a neighboring molecule – his research has taken him into the areas of cell motility and cancer research.

Dr Leavis, who has made many significant contributions in the field of muscle proteins with his past publications, has now applied his expertise in protein chemistry to the development of a novel screening technique to discover new factors that regulate cell growth. As you will read, these newly discovered substances have tremendous potential to be developed as new therapeutics for the treatment of cancer.

To those of you who have been loyal supporters of the BBRI, I hope you will continue to share in the excitement and fascination that accompanies the ongoing development of these scientific stories – and, I thank you! To those of you who are new to the BBRI and would like to hear more, I welcome you and invite you to join me for a tour of our facilities!

Kathleen G. Morgan, Ph.D.

BOSTON BIOMEDICAL RESEARCH INSTITUTE

BY-LAWS

[as amended through November 15, 2001]

separate affirmative vote of the Trustees and Faculty, taken one year prior to the expiration of the Director's term.

The Deputy Director shall be appointed annually by and from the Faculty for a one-year term, upon recommendation of the Director.

Section 3. Assistant Officers. The Board of Trustees may appoint an Assistant Treasurer, an Assistant Secretary-Clerk and such administrative officers as it may from time to time believe necessary. Such additional officers need not be members of the Corporation. They shall serve from the time of their appointment until the first meeting of the Board following the next succeeding Annual Meeting.

Section 4. Vacancies. Any vacancy occurring in the office of any of the officers of the Corporation, except that of the Director and the Deputy Director, may be filled at any time by the Board of Trustees, and any person elected to fill such a vacancy shall hold office for the remainder of the term of the Officer whose place he/she takes. In the event of a vacancy in the office of Director, the Deputy Director shall assume the office until such time as the Trustees appoint an acting Director. If the Deputy Director shall resign or be or become unable to serve for the remainder of the term, the Director, after consultation with the Committee on Research, may appoint an interim Deputy Director who shall assume the office for the remainder of the term.

Section 5. Number of Offices Held. Except as otherwise specifically required by law or as otherwise specifically provided by these By-laws any person may hold two or more offices in the Corporation at the same time.

ARTICLE V

FACULTY

Section 1. Faculty. All Staff Scientists holding appointments for terms of not less than three (3) years shall constitute the Faculty. It shall from time to time advise the Committee on Research on matters relating to the scientific and educational activities of the Corporation, except as otherwise provided in these By-laws.

Section 2. Tenure.

A. The Board of Trustees may from time to time grant an appointment with tenure to a staff scientist at the Institute. Such appointments shall be made only on the recommendation of an ad hoc tenure committee to be appointed by the Board of Trustees, and with the approval of two-thirds of the members of the Committee on Research.

B. **Tenure, as such term is used in the By-laws, shall mean a permanent appointment to the staff of the Institute and a guarantee of the reasonable use of the research laboratories or other facilities of the Institute consistent with the research funding available to the staff member subject to the following conditions:**

1. Tenure shall terminate on retirement or upon resignation of the staff scientist or pursuant to revocation for grave misconduct or neglect of duty by a vote of two-thirds of the members of the Board of Trustees, upon the recommendation of the Committee on Research.
2. Tenure may be withdrawn by the Board of Trustees upon recommendation of two-thirds of the members of the Committee on Research if the research being conducted by that individual becomes inconsistent with the research program of the Institute.
3. Such further conditions as may be imposed by the Committee on Research in individual cases.
4. All determinations by the Board of Trustees hereunder shall be final and binding on all persons.

ARTICLE VI

DUTIES OF OFFICERS

Section 1. Chairman. The Chairman shall be the senior officer of the Corporation. He/she shall cause to be prepared the agenda of the Annual Meeting and of all special meetings of the Corporation in cooperation with the Director, and he/she shall preside at all meetings of the Corporation. In addition, he/she shall perform such other special duties as from time to time may be determined by the members of the Corporation.

Section 2. President. The President shall preside at the meetings of the Board of Trustees, and he/she shall cause to be prepared the agenda of the meetings of said Board in cooperation with the Director.

Section 3. Vice Presidents. The Vice Presidents shall assist the President in the performance of his/her duties and shall act for the President in the latter's absence.

Section 4. Director. The Director shall be the chief executive officer of the Corporation. He/she shall report to and carry out the general policies established by the Board of Trustees, which shall regularly review the performance of the Director. As chief executive officer he/she shall be responsible for the direction, management and implementation of the scientific and educational activities and policies of the Corporation consonant with the determinations of the Committee on Research with respect to all matters related to such activities. In addition, he/she shall perform such other duties and have such other powers as the Board of Trustees may from time to time determine. The Director shall preside at the meetings of the Committee on Research.

Section 5. Deputy Director. The Deputy Director shall assist the Director in the performance of his/her duties and in his/her absence shall act for the Director.

BOSTON BIOMEDICAL RESEARCH INSTITUTE

Victor A. Raso, Ph.D.

20 STANIFORD STREET, BOSTON, MASSACHUSETTS 02114
Area code 617 • 742-2010
Telefax 617 • 523-6649

November 21, 1996

To The Members of The Committee On Research:

At the end of November funds will run out on a 6-month Small Business Innovation Research Grant "Catalytic Antibodies for the Treatment of AIDS." This money (99,911 - 38,174 BBRI service fee) has been sustaining my laboratory following the finish of institutional support. Unfortunately, it now appears that the re-submitted competing continuation of my NIH grant "Targeting Toxins with Acid-Triggered Hybrid Antibodies" will not be funded this round. I am therefore writing to request institutional funds for second year support to temporarily operate the laboratory (one year salary plus supplies) while NIH and other funding is being sought.

The prospects for future support are as follows:

1. Experiments are underway to obtain data for second phase funding of the recently awarded 6-month Small Business Innovation Research Grant "Catalytic Antibodies for the Treatment of AIDS".
2. A similar NIH R01 grant "~~Catalytic Antibodies Directed Against HIV~~" will also be submitted.
3. My NIH grant "Targeting Toxins with Acid-Triggered Hybrid Antibodies" will either be re-submitted for competing renewal or more-likely will be revised as a new grant "Targeting Binary Toxins" to better reflect its renovated scientific direction.
4. A new NIH grant "Amyloid β -Peptide Equilibria in Alzheimer's Mice" is currently being written. ✓
5. A related grant, "Catalytic Antibodies for the Treatment of Alzheimer's Disease" will be submitted as an SBIR grant and also to the Alzheimer's Association. ✓

Given the scope and relevance of the topics addressed, I believe that at least one of these grants will be funded.

To help strengthen the competing renewal grant application, I have submitted two manuscripts that are currently being reviewed by the *Journal of Biological Chemistry*.

I believe that I have made a positive contribution to the BBRI over the years and with eventual funding hope to do so in the future. While the "fit" of my research may not be ideal in the current scheme of things, it has always been on the cutting edge of biomedical research and has excited interest among our non-scientist supporters.

With regard to personnel, Christine Kearney is currently providing essential technical assistance on the AIDS, cancer therapy and Alzheimer's disease projects in addition to maintaining the smooth operation of all laboratory support functions. I will utilize my salary to keep Christine working at the BBRI.

Sincerely,

A handwritten signature in black ink that reads "Vic Raso". The signature is stylized, with the first letters of the first and last names being capitalized and prominent. There is a long, sweeping horizontal stroke at the end of the signature.

Vic Raso, Ph.D.

November 21, 1996

BRIDGE SUPPORT

FIRST YEAR

- A first year of bridge support in an amount equal to the PI's salary is given to productive members of the faculty contingent upon timely submission of competitive grant applications.
- The amount of bridge support is proportional to the percentage of the PI's time allocated to the specific grant whose funding is delayed.
- If funding is received before bridge support runs out, unused moneys will be returned to the Institute.
- New faculty are required to have used all of their seed money before being eligible to request bridge funding and to have successfully brought in a grant submitted from the BBRI in order to be eligible.
- Application does not require submission of pink sheets and scores but does require a financial statement.
- For faculty members who have previously received bridge support, a new round of bridge support can only be obtained after successfully obtaining a full RO1-type grant (e.g. NIH, NSF, SBIR) of three years or longer, or comparable support.

SECOND YEAR

- Only available in exceptional circumstances until additional sources of revenue are available to the Institute.
- PI must submit to the COR with the application for a second year of support:
 - Scores and pink sheets from most recent NIH review
 - CV
 - Letter outlining the PI's plan for successfully building his/her program and obtaining funding
- Criteria to be used in making decision of whether to recommend second year of bridge support:
 - Probability of funding
 - Excellence of science
 - Contributions to Institute
 - Programmatic fit

BOSTON BIOMEDICAL RESEARCH INSTITUTE

COMMITTEE ON RESEARCH

November 27, 1996

A regular meeting of the Committee on Research was held on Wednesday, November ²⁷~~28~~, 1996, at 10:00 a.m. Present at the meeting were Drs. Morgan, Grabarek, Paulus, Raso, and Wang. Others present were Mr. Thomas McQuaid, and Ms. Barbara Zillman, who recorded the proceedings.

1. Dr. Morgan asked for approval of the minutes of October 29, 1996. Clarification was requested on three items. They were as follows:

1) In item 5, concerning Dr. Volloch, the term "bridge support" is inaccurate and should be redefined as "R21 support." 2) Same sentence, the term "scientific misconduct" is inaccurate and should be restated as "alleged misconduct...." 3) In item 6, concerning potential BBRI floor space, the discussion is more accurately reflected with the following addition after the phrase ".....room itself belongs to BBRI.": "Dr. Grabarek asked if the room is available immediately and Mr. McQuaid replied that it is not."

With these clarifications noted, it was

VOTED: Unanimously, to approve the minutes of October 29, 1996.

Following this vote, Dr. Morgan recapped for the record, because of subsequent events, the intent of the C.O.R., at its last meeting, to provide Dr. Volloch with temporary laboratory space following his relocation from the second floor. Dr. Leavis had volunteered to clear one and one-half of his own benches for use by Dr. Volloch, with the understanding that if Dr. Leavis was awarded his then-pending grant application, his space would be returned. Dr. Leavis has since learned that his grant application has been awarded and he will need to reclaim his lab for expansion of his program. The ESR room in the basement was made available, temporarily, to Dr. Volloch by Dr. Graceffa. Dr. Graceffa and Dr. Gergely are composing a letter to Dr. Volloch stating that he is to vacate the ESR room by a specified date and that while occupying it, there are not to be radioactives used in that room, and that the equipment must not be harmed. C.O.R. members agreed with the appropriateness of giving Dr. Volloch such a letter. The following issues were reiterated: the allocation of space in the basement to Dr. Volloch is temporary; the C.O.R. as a body, and each member individually, must work to see that Dr. Volloch submits a follow-up competitive renewal grant application to the NIH - the conditions of the R21 that Dr. Volloch received require this and assure expedited review if he submits his application on time; the C.O.R. must consider upon submission of that grant application, what to do next. The decision concerning his application should be known in July. If triaged, Dr. Volloch will be asked to leave the Institute but if funded, he may be allowed to stay. Funding must be from the NIH; an Alzheimer's grant would not be enough. If asked to leave, he is to be given advance notice (if outcome is in July, notification would be for relocation in September). In any case, he has been made no promise as to continued lab or office space beyond his current funding. If during his accelerated review, his score is in the top 30%, he will be allowed to resubmit his application for the summer deadline.

2. The next item of discussion was setting a policy on misconduct proceedings. There was some discussion about this topic and it was agreed to continue without formal policy implementation.

3. Proposals were discussed next. The first was that of Dr. Coleman.

Dr. Coleman has made a request for his first year of bridge support (see attached). Using the current guidelines for granting requests for bridge support, Dr. Coleman was evaluated on several items and concerns were raised by C.O.R. members. Dr. Grabarek noted that Dr. Coleman has not been active in publishing since 1994. Dr. Paulus noted that Dr. Coleman had been appointed to a faculty position at the Institute with two active NIH grants, and never re-applied for the grants when they

expired. Further, he has made himself very part-time at the Institute. A formal vote by the C.O.R. in October, 1991 guaranteed him a salary for three years, contingent upon his funding. Dr. Coleman now has no funding. C.O.R. members concluded that by current guidelines as well as the vote of the C.O.R. in October, 1991, Dr. Coleman does not qualify for full bridge support. Some further discussion took place and it was moved, and by a majority,

VOTED: Because of questions of productivity and failure to renew grant applications in a timely fashion, but because of past contributions to the Institute, three months salary support will be awarded to Dr. Coleman, using his base salary of \$70,000. This is consistent with the determination of the October 2, 1991 meeting of the C.O.R.


There were four aye votes and one ~~no~~ ^{abstention by Dr. Vaso} vote.

The second proposal to be discussed was that of Dr. Raso. He left the room while discussions took place.

Dr. Raso is requesting his second year of bridge support (see attached). His first year of support was awarded before the current criteria were established and his first year of support was very generous. The merits of Dr. Raso's proposal were deemed to be that he had brought in over a \$1,000,000 in overhead to the Institute. Furthermore, Dr. Raso has viable patents and is very technology-oriented, a future direction the Institute will take, and a probable revenue stream. The negative aspects of the proposal were considered to be a lack of publications. The amount to be requested was further refined by again referring to current criteria. Dr. Raso has already received an equivalent of 16 months of support, including supplies, in his first year of support. Therefore, a financial commitment of eight months will be made to him. It was,

VOTED: Unanimously, to request a second year of bridge support for Dr. Raso from the Board in an amount equivalent to eight months of both salary and supplies (at \$10,000 per year), and to allow that amount to be awarded effective immediately. This vote is subject to reversal by the Board at its next meeting in January, 1997. ^{approved}

4. There being no Other Business, the meeting was adjourned at 1:35 p.m.


Barbara Zillman

December 9, 1996



ILEEN G. MORGAN, Ph.D.
DIRECTOR

42-2010
27-6053 FAX
li: morgan@bbri.cri.harvard.edu



September 24, 1997

Victor A. Raso, Ph.D.
Senior Scientist
Boston Biomedical Research Institute
20 Staniford Street
Boston, MA 02114

Dear Vic:

As you know, your current appointment as a senior scientist at the BBRI extends for another two years. The Institute, however, does have a policy of reviewing appointments for senior scientists two years in advance, to provide warning if there is any possibility that the appointment may not be renewed. At this point I am writing to give you such warning. Given your current string of bad luck at the NIH, it may possibly be necessary for us to vote against renewal of your appointment two years from this date.

I was very pleased to discover today that you had recently succeeded in publishing two new papers in JBC. Congratulations! This should help you in your grant applications and it's my hope that successful funding of NIH or other similar grants will allow us to renew your appointment when the time comes.

You should be aware that the allocation of space is separate from the academic appointment but is also linked to the availability of funds for utilization of lab space. I hope that you will be willing to share any hint of good news with us as soon as you receive word on your grants.

Sincerely yours,

Kathleen G. Morgan, Ph.D.
for the Committee on Research

KGM/mfd

a/mtgs.../cor.raso

20 STANIFORD STREET, BOSTON, MA 02114

Kathleen Morgan, 12:54 PM 4/10/98 , No Subject

VIC RASO

PERSONNEL FIL

Date: Fri, 10 Apr 1998 12:54:18 +0100

To: Raso

From: Kathleen Morgan <morgan@bbri.harvard.edu>

Cc: mcquaid@bbri.harvard.edu (Thomas J. McQuaid)

Vic--Just so there is no mis-communication. . . I wanted to confirm our discussion from earlier in the week. Since your SBIR will only run 6 months, doesn't really cover overhead and there's no sign of an RO-1 coming in in the foreseeable future, I will need to be bringing search candidates through your space, indicating that the space will be available for new faculty members.

However, we can make some space available for you in the basement and there is no need to move until the end of June. Of course, if you get a fundable score on one of your pending application in the June study sections--or any other possible source of support, please let me know ASAP.

Keeping my fingers crossed.

Kathy



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Victor Raso
Application No.: 09/992,994
Filing Date: November 6, 2001
Title: IMMUNOLOGICAL CONTROL OF β -AMYLOID LEVELS *IN VIVO*
Art Unit: 1652
Examiner: Patterson, C.

DECLARATION OF ALAN L. KAYE, CPA

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Alan L. Kaye, do hereby declare and say:

1. I am the Chief Financial and Administrative Officer of the Boston Biomedical Research Institute (BBRI). I am in charge of all financial and administrative matters of the BBRI. I have reviewed the personnel file of Vic Raso, a Senior Scientist, without tenure, at the BBRI, as well as the financial and other administrative records relating to Vic, his laboratory, and his grants. Although I did not join the BBRI until 2000, these records for 1996-1999 were the records the BBRI kept, and continues to keep, in the ordinary course of its business.

2. The BBRI is an independent, not-for-profit biomedical research institute. As such, it is dependent upon federal grants, principally from the National Institutes of Health (NIH), for its revenues. The typical NIH grant received by BBRI (an RO1)

provides the BBRI with direct costs for the research project (salaries, supplies, etc.) and, indirect costs (overhead costs, such as light, heat, administrative services, etc.) [Ex. A at p. 7]. With few exceptions, the salaries of BBRI faculty are paid by such grants as direct costs. BBRI faculty are expected to be self-funded, generating their income via such grants.

3. While the BBRI depends upon grants to pay faculty salaries as direct costs, such grants are also very important to the BBRI because they fund the overall budget as indirect costs. Otherwise, the grant would not reimburse BBRI for the cost of the entire project [Ex. A at p. 4]. As Chief Financial and Administrative Officer, I am particularly aware of the drawbacks of grants that do not include indirect costs. Each time the BBRI accepts such a grant, it is essentially losing money.

4. Because BBRI faculty are expected to be self-funded, they are expected to generate new grants regularly. BBRI faculty hold appointments of three, four, or five years for Scientists, Principal Scientists, and Senior Scientists, respectively [Ex. B at p. B-06a]. Reappointment to an additional term is dependent upon four criteria. The primary criteria is grant support [Ex. B at p. B-03]. In certain cases, however, BBRI will award tenure to faculty members, resulting in a permanent appointment [Ex. C at p. 4].

5. Vic joined the BBRI in 1988, receiving an appointment as a Visiting Scientist [Ex. D]. That appointment was for one year and, as Vic's offer letter indicated, his salary was contingent on his ability to generate outside funding. Vic then joined the faculty of the BBRI as a Senior Scientist in 1989 [Ex. E]. That appointment was for five years and, as Vic's offer letter indicated, his salary was contingent on his ability to generate outside funding. At the end of that appointment, Vic was reappointed as a Senior

Scientist in 1994 [Ex. F]. Again, that appointment was for five years and, as Vic's offer letter indicated, his salary was contingent on his ability to generate outside funding. None of Vic's appointments were tenured.

6. The BBRI provides temporary funding to faculty members who are thought to be likely to regain funding [Ex. G at p. A-21; Ex. A at p.3]. Such Bridge Support is available for only one year, other than in "exceptional circumstances" [Ex. B at p. E-06]. The primary criteria for determining whether such an exceptional circumstance existed is the probability of funding [Ex. B at p. E-06].

7. Vic's records indicate that he was already on Bridge Support when the BBRI formalized its policy. He requested a second year of Bridge Support in late 1996. In support of his request, he indicated that he was actively working on five different grant applications [Ex. H at p. 1]. Although he did not appear to meet the new criteria, BBRI approved further Bridge Support, although for only eight months, not a full year [Ex. I at p. 2].

8. Vic continued to seek funding. His many and repeated efforts were not successful, however. Vic even tried to obtain other sources of funding, seeking Small Business Innovation Research Grants, as well as grants from the Alzheimer's Association. Having failed to get the typical NIH grants, Vic tried these sources even though he knew the BBRI was not terribly interested in such grants because such grants do not provide indirect costs. Indeed, Vic was a member of the Committee on Research (COR) that voted to grant contingent Bridge Support to a faculty member [Ex. I at p. 1]. That vote was contingent on the faculty member obtaining NIH funding. The

COR specifically stated that “an Alzheimer’s [Association] grant would not be enough” [Ex. I at p. 1].

9. Vic’s Bridge Support was not sufficient to keep his laboratory running. He maintained his technician in 1997 by cutting his salary to pay for her salary [Ex. J at p. 1]. Vic indicated he believed it was particularly important to keep his technician to obtain the data for the grants he was writing. Indeed, he noted that he could not do the lab work because he was “increasingly pulled away from the laboratory to write grants and papers” [Ex. J at p. 2].

10. Vic continued to fail to obtain funding. Therefore, in September 1997, the Director of the BBRI formally warned him, pursuant to the BBRI’s Faculty Reappointment Policy, that he might not be reappointed as a Senior Scientist when his term ran out in two years [Ex. K]. The Director indicated that his continued failure to obtain NIH grants might cause the BBRI to not renew his appointment. She also told him that, if he could obtain “NIH or similar grants,” he might be reappointed in two years [Ex. K].

11. BBRI allocates laboratory space based upon funding and utilization levels [Ex. B at p. G-17]. Besides warning Vic that he might not be reappointed, the Director’s letter also reminded him of this policy [Ex. K]. Separate from Vic’s academic appointment as a Senior Scientist, if he did not have funding, he was at risk of losing some or all of his laboratory space. This did happen to Vic so that, by late 1999, he had lost all his space except for one-half a laboratory bench and his office. Vic’s lost laboratory space was remodeled for a new faculty member.

12. The BBRI requires monthly Time and Effort Reports of all faculty members [Ex. B at p. A-06]. The reports show the percentage of time spent on each fund. Funds normally correspond to particular grants received by the faculty member. Vic's Bridge Support ended on September 15, 1997. At that time, Vic's Time and Effort reports switched from "Institutional Support" to "Grant Writing." Vic's Time and Effort Reports indicate that he spent all his time preparing grants from the end of his Bridge Support on September 15, 1997, through December 31, 1997.

13. Vic was terminated at the end of 1997 because he did not have any funds to support his work [Ex. L; Ex. M]. Upon termination, Vic was no longer eligible for health insurance through BBRI. As a faculty member, however, Vic was still entitled to use BBRI facilities until such time as his laboratory space was allocated to another, funded faculty member.

14. In April 1998, Vic obtained a SBIR grant. Such a grant is of short duration and did not cover overhead. Accordingly, the Director met with Vic and informed him that she would be bringing faculty candidates by to look at his laboratory space, indicating that it would be available for them [Ex. N].


15. The BBRI had some laboratory space in the basement, which was generally the least desired. Faculty members who were transitioning out of the BBRI were sometimes placed there temporarily. Indeed, the faculty member mentioned above whom the COR voted contingent bridge support was moved to that space before leaving the BBRI. The Director indicated to Vic that BBRI could make some space available for him there [Ex. N].

16. Vic's personnel files and the BBRI's grant files indicate that Vic was apparently constantly working on grant applications. From January 1997 until August 1999, he prepared and submitted 16 grant applications. These 16 grant applications all concerned Alzheimer's Disease, particularly the use of antibodies to β -amyloid:

Date	Type of Grant (Form)	Title	Bates Number
01/15/1997	NIH (PHS 398)	AMYLOID β PEPTIDE EQUILIBRIA IN "ALZHEIMER'S MICE"	B000030
08/29/1997	NIH; SBIR (6246-1)	IMMUNOTHERAPY OF ALZHEIMER'S DISEASE	B000093
10/21/1997	NIH (PHS 398)	AMYLOID β PEPTIDE EQUILIBRIA IN "ALZHEIMER'S MICE"	B000223
12/11/1997	NIH; SBIR (PHS 6246-1)	CEREBRAL ANTIBODY DELIVERY TO TREAT ALZHEIMER'S DISEASE	B00269A-269Y
01/26/1998	NIH (PHS 398)	CEREBRAL DELIVERY OF VECTORIZED ANTI- β -AMYLOID ANTIBODY	B000270-312
04/13/1998	NIH; SBIR (PHS 6246-1)	CATALYTIC ANTIBODIES TO INACTIVATE β -AMYLOID	B000313-339
05/20/1998	NIH (PHS 398)	VACCINE TO MODULATE SYSTEMIC β -AMYLOID LEVELS	B000340-365
05/27/1998	NIH (PHS 398)	PROBE TO VISUALIZE CEREBRAL β -AMYLOID PLAQUES	B000366-392
09/01/1998	Alzheimer's Association (KRS)	VACCINE TO MODULATE (SYSTEMIC) BETA-AMYLOID LEVELS	B000432-449
09/03/1998	Alzheimer's Association (KRS)	CEREBRAL DELIVERY OF VECTORIZED ANTI- β -AMYLOID ANTIBODY	B000393-413
09/04/1998	Alzheimer's Association (KRS)	CATALYTIC ANTIBODIES TO INACTIVATE β -AMYLOID	B000414-431
10/11/1998	NIH (PHS 398)	CEREBRAL DELIVERY OF VECTORIZED ANTI-BETA-AMYLOID ANTIBODY	B000476-523
01/19/1999	NIH (PHS 398)	IMMUNOTHERAPEUTIC AGENTS TO TREAT ALZHEIMER'S DISEASE	B000141
01/27/1999	NIH (PHS 398)	NOVEL TRANSITION STATE PEPTIDE ANALOG ANTIGENS	B000524-569
04/12/1999	NIH; SBIR (PHS 6246-1)	BIPHASIC PROBE TO VISUALIZE INTRACELLULAR BETA-AMYLOID	B000450
08/13/1999	NIH; SBIR II (PHS 6246-2)	IMMUNOTHERAPY OF ALZHEIMER'S DISEASE	B000187

17. In my experience at BBRI, this is truly a phenomenal number of grant applications to prepare and submit in about 2 ½ years. The NIH's guidelines indicate that each grant application should take three to six months to write [Ex. O]. For Vic to be submitting so many grant applications during this period, he had to have been working on them non-stop. That is consistent with his Time and Effort Reports up until his termination by the BBRI.

I understand that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the above-identified patent.


Alan L. Kaye, CPA

BOSTON BIOMEDICAL RESEARCH INSTITUTE
Program for the Future

STRATEGIC PLAN OUTLINE

SCIENTIFIC PROGRAM

- I. **Faculty Development**
 - A. New Faculty Recruitment
 - B. Bridge Support
 - C. Fringe Funding
 - D. Unreimbursed Indirect Costs
 - E. Scientific Support Initiative
- II. **Capital Equipment**
 - A. Structural Biology Facility
 - B. Protein Expression Facility
- III. **Space**

BUSINESS PROGRAM

- I. **Revenues**
 - A. Grants (Faculty-Initiated)
 - 1. Federal
 - 2. Other Agencies (Non-Federal)
 - 3. Pharmaceutical/Industrial Collaborations
 - B. Development/Public Relations
 - C. Investments
 - D. Technology Transfer
- II. **Expenses**
 - A. Directs
 - B. Indirects

BOSTON BIOMEDICAL RESEARCH INSTITUTE
Program for the Future

STRATEGIC PLAN

SCIENTIFIC PROGRAM

I. Faculty Development

The long-range scientific strategy is to build upon our current reputation as the center for *muscle research* in the Boston community by not only further developing this area of investigation but also developing two additional interacting areas of research excellence. These two additional areas will be *cellular communication* and *cellular growth*. By developing strong basic science programs in these three overlapping specialties, we will have the necessary depth and scope to be able to make major contributions to health issues such as stroke, heart failure, and hypertension.

In the area of *muscle research*, additional scientists in the field of nonmuscle motility should be recruited. The successful recruitment of scientists working on novel molecular motors and on cytoskeletal-matrix interactions in nonmuscle cells will allow the Institute to apply its half-century of expertise in contractile proteins to much broader questions such as the "crawling" of cancer cells during metastasis and the trafficking of messages within cells. Thus, these scientists should be able to interact not only with the muscle group, but also the cell growth group and the cell communication group.

In the area of *cell communication*, the Institute already has considerable expertise in the area of transport proteins, and the recruitment of a channel person with patch clamp and perhaps channel cloning abilities would allow focused research on transmembrane communication in a much broader sense and in a manner that could greatly enhance investigations into motility and cell growth. Additionally, the recruitment of molecular biologists working on kinases and signalling cascades in both differentiated and proliferative smooth muscle cells would strengthen this focus group and assure interactions with the muscle and cell growth groups.

In the area of *cell growth*, the recruitment of a cell-cycle person or a growth factor person could greatly increase relevance of ongoing research into DNA and RNA replication mechanisms and would enhance the possible collaborative interactions of the muscle and cell communication groups.

A. New Faculty Recruitment

In the current era of financial crisis in biomedical research, fewer and fewer young graduates are entering basic research. This has created an intense competition among academic institutions for the best and brightest scientific graduates. At the same time, given the current shortage of federal funds for support of scientific

research, it is exceedingly difficult for the new scientist to become established as a recognized expert in a field of investigation and thus successfully compete for federal funds. Only the best of the young scientists do succeed and, on average, three to five years appears to be required for the new individual to become entirely self supporting. For this reason, the most competitive research centers are now offering five year packages of guaranteed support during the recruitment process. BBRI currently has the financial means to offer support for only two to three years, thus decreasing our competitiveness in recruiting new faculty and also, in some instances, forcing us to terminate promising young individuals before we have the opportunity to see any return on our initial investment. Supplementation of current resources by the creation of named Young Scientist Awards would greatly increase our chances of recruiting and retaining top investigators.

Estimated costs for recruiting two new Principal Investigators each year are: PI's salary $\$60K \times 2 = \$120K$; Tech $\$25K \times 2 = \$50K$; Salaries = $\$170K$; $\times 2.6$ indirects and fringes = $\$442K$; Start-up = $\$40K$; Supplies $\$10K \times 2 = 20K$; Relocation and remodeling = $\$30K$. Total: $\$532K$. Current estimates indicate that we should recruit two scientists per year in order to optimize grant income and maintain the vitality of the scientific programs.

B. Bridge Support

An equally urgent need is bridge funding of established investigators to cover the inevitable intervals when federal funding is delayed. A general goal will be to decrease the excessive dependence on NIH and similar sources for funding. Although federal funds will undoubtedly remain the main support for basic research, efforts should be made to create a "mixed portfolio" including industrial contracts, pharmaceutical and clinical collaborations, foundation support, and endowed, named Senior Scientist Awards. The interest on BBRI's endowment should be a major source for bridge funding, hence the importance of maintaining and increasing the current principal. Current experience indicates that providing bridge support for investigators averages $\$225,000$ annually.

We currently have the resources to provide support equal to the Principal Investigator's salary for one year. This policy inevitably results in loss of valuable intellectual capital. The long range goal is to develop resources to provide up to two years of support for the Principal Investigator and one member of the research team.

C. Fringe Funding

Currently, most of a Principal Investigator's time is focused on acquiring and maintaining NIH support. It is generally acknowledged that the NIH will only support ideas that are clearly documented to be entirely "feasible" by the presentation of considerable "preliminary data" and demonstrating that pilot studies have already been successfully performed. Truly novel and creative ideas cannot be supported by this mechanism and as a result the true potential of the

"intellectual capital" of the Institute is not being tapped. Hence there is a need for a funding mechanism to support ideas on the "fringe" of established concepts and pilot studies that will provide preliminary data that will eventually lead to NIH support. No funds are budgeted in this five-year period for this program, but fundraising efforts by the Development team could be focused on creating such a program.

D. Unreimbursed Indirect Costs

There are a number of agencies that provide grant funding that does not include indirect costs or, in other words, grants that do not reimburse the Institute for the cost of the entire project. Many of these grants, however, are highly prestigious and it is greatly to BBRI's advantage to have our faculty receive such awards. It is necessary, therefore, for BBRI to anticipate allocating funds to cover the unreimbursed indirect costs associated with these research projects. This currently involves the use of about \$150,000 of Institute funds annually for sharing incompletely reimbursed indirect costs.

E. Scientific Support Initiative

It is also imperative that BBRI initiate an outreach program to attract the necessary support resources for BBRI's scientists, e.g. students from local colleges and universities; post doctoral fellows; M.D.s in specialty training programs; visiting scientists; etc. BBRI offers a unique and ideal environment in which these talented young people can begin to explore or continue to build a career in basic research and our scientists will benefit from the additional research support as much as these individuals will benefit from the experience and the expertise at BBRI. It is equally important, however, that this initiative be implemented and maintained with minimal cost to the Institute.

II. Capital Equipment

A. Structural Biology Facility (attached)

B. Protein Expression Facility

Certain molecular biology techniques have now been sufficiently established to have become routine. In order to promote efficient utilization of BBRI resources and to capitalize on the collaborative nature of the Institute, efforts will be made to prevent the duplication of facilities that can be centralized and shared.

There is an immediate need for expression of proteins in essentially all BBRI laboratories. Rather than have each investigator independently devote personnel and time to a routine procedure, the Institute will set up a shared Protein Expression Facility. A Core Leader--a Principal Investigator-- will contribute 10% of his/her time to supervise the facility. A full-time research technician will be responsible for

day-to-day operations. Two-four large capacity incubators/shakers and two laminar flow hoods will be located in a small, self-contained laboratory. The core will be responsible for producing proteins primarily by using the baculovirus expression system, including keeping the virus stock, making the constructs, maintaining insect cell cultures, performing co-transfection and scaled-up production of proteins.

Funding for the core facility will be sought as part of the Smooth Muscle Program Project Grant (PPG), a competitive renewal grant to the NIH, and therefore will require minimal institutional funds.

III. Space

The current space available at BBRI allows the recruitment of only two additional investigators with rather modest space needs. Improving the air circulation and lighting in the basement and rearranging the existing space can optimize its use but, if the Institute is truly to be able to grow in the next millennium, some plan of action will have to be created for additional space.

BBRI still benefits from the lease negotiated with Schepens 25 years ago. In effect, BBRI does not pay for floor space itself but shares in the operating costs as outlined above. Operating costs are higher than those in a modern facility due to the inefficiencies inherent in an older facility. However, our per square foot cost of occupancy is considerably lower than at alternate sights.

The Institute has considered purchasing or leasing a different site for the facility. The lease does not allow BBRI to sublet space at Staniford Street, effectively limiting our sales market to Schepens Eye Research Institute. Although we know Schepens is seeking additional space, we feel it is unlikely that they will be prepared to offer us enough incentive to vacate. Economically, we can continue to enjoy the facility "rent free" for the next 25 years. It may be possible to renew the current lease but whether this would be a feasible, or desirable, option depends on the plans of the SERI, the condition of the building and the details of the new lease. Current strategic plans of the SERI appear to preclude extending the existing lease. It is to be recognized, however, that any plans to build onto the current building must be contingent on the eventual extension of the current lease.

Within the five-year Strategic Plan, we have factored in the following plans for the provision of adequate space.

Rental: Additional space could be rented in neighboring buildings. This could be done at a cost of \$25/sq. ft. in the Charles River Plaza or the building at 50 Staniford Street. For fiscal year 1997, we are considering renting 1,000 square feet and relocating the Accounting and Development offices to this space. The current Accounting Office area would then be renovated to accomodate the X-ray crytallography equipment and program staff.

For fiscal year 1998, two plans have been developed. The first would be in anticipation of the natural attrition in any organization and would focus on recruiting new faculty to use the space that would be vacated in the process of attrition. The second plan would be to rent additional space in the Charles River Plaza. Again, rental of this space would be \$25/square foot and it is likely we would be required to rent a minimum of 2,000 square feet initially, for a total of \$50,000 annually. Renovation of that space would require roughly \$120/sq. ft. If we assume a new investigator requires approximately 400 square feet, the initial construction cost for a laboratory would be \$50,000. The close proximity would allow for use of shared equipment and interaction with other faculty.

Looking ahead, beyond the five-year Strategic Plan, the decision remains to be made regarding relocation of the entire Institute.

Relocation: The entire Institute could relocate. This would be by far the most costly and time consuming option but should be considered an option for long term planning. Alternative laboratory space is available in other areas of the city. For example, laboratory space in the Longwood Medical Area rents for about \$55 per square foot (\$22,000 annually for a 400 square foot lab), with the advantage of proximity to Harvard University personnel and affiliates.

One specific concern is the fact that although the Institute has the academic prominence to host major international conferences, there is currently no on-site auditorium of the necessary size for such a venture. If funds could be obtained, a named conference center would significantly enhance the mission of the Institute to discover and disseminate new biological knowledge.

BUSINESS PROGRAM

The remarkable track record of success of the faculty in bringing in 90% of expenses from grants is a credit to their level of scientific excellence. At the present time, the Institute receives roughly 90% of its operating budget from these grants, the majority of which come from the NIH. Given the current shortage of funds at the NIH, allowing only 9-15% of meritorious grants to be funded, a major goal over the next decade will be to create a more "mixed" portfolio, which will reduce the Institute's dependence on faculty-initiated grants from the NIH and similar agencies and increase the supporting income from long and short term industrial contracts, foundation support, private donations, and return on BBRI investments to approximately 40% of the budget.

I. Revenues

A. Grants (Faculty-Initiated)

1. Federal

The U.S. government is the single largest supporter of biomedical research in the world; in 1994, the U.S. spent about \$33 billion for biomedical and related health research and development. The federal government provides approximately 80% of the monies spent each year for biomedical research at universities, medical schools, and not-for-profit research institutes. 87% of all federal support for biomedical research comes from funds allocated by Congress to the National Institutes of Health (NIH); the 1995 NIH budget was \$11.3 billion.

The NIH continues to be BBRI's major source of grant funding. Occasionally, the Insitutute also obtains funding from the National Science Foundation (NSF). The typical Individual Investigator Initiated Research Project Grant, termed RO1, provides BBRI with direct research costs (salaries, research supplies, etc.) and indirect costs (i.e. those costs incurred by BBRI such as light, heat, administrative services, etc.).

The grant process at NIH is a long, stressful process for the scientist who has submitted a grant. The NIH receives grant applications 3 times a year. The applications are generally 30-50 page documents and require that all proposed experiments be accompanied by preliminary experiments to certify feasibility. Approximately 3-4 months after receipt, the grants are subjected to "peer review" by one of several "Study Sections", i.e. a committee of scientists from across the country that meets in Bethesda, MD. for 2-3 days to construct a relative ranking of the grants by merit. Currently, 4 of our faculty members serve on NIH Study Sections as nationally recognized experts in their fields.

The study section assigns a "priority score" from 1.00 to 5.00 to each grant—with 1.00 being most meritorious and 5.00 being least meritorious. Recently, in an effort to decrease administrative cost and time, a "triage" process has been implemented and grants that are evaluated to be in the worse half (generally scores of 2.5 and larger) do not receive full review by the committee or a score.

When the study section completes its evaluations, the scores are "percentiled" against past scores recommended by that individual study section. Only percentiles are compared between study sections, in order to normalize for differences in the generosity or toughness of scientists on the individual study sections.

Three to four months after the study sections complete their work, the grants receive a second level of review by the Councils of the NIH. Each Council will set a "payline". Current paylines are ranging from 9-15%. Often a grant is borderline and, also because of political uncertainties, the Principal Investigator may not know for sure whether he or she is funded until shortly before the start date of the grant, 3-4 months after Council meets. Thus there is significant lag (generally 9 months) between submission and funding of successful grants.

Because of the shortage of funding for excellent grants, most investigators expect to need to revise their applications at least once, adding another 9 months to the delay in funding. Current efforts are being made to try to submit renewal applications for funding one year early in an effort to keep programs (and personnel) continuous.

2. Other Agencies (Non-Federal)

There are several private national foundations to which investigators can apply for support. However, these sources require that the research be disease-oriented. Also, these grants are relatively small in dollar amount, and they do not provide continuous support of ongoing investigations. These smaller grants can be very useful, however, in adding needed personnel to a project or in providing support of an ongoing project while waiting for NIH funding to be awarded.

The Institute has received, and continues to receive, generous support from the Muscular Dystrophy Association for its work on muscle disease, from the American Heart Association for its work on stroke, heart failure and hypertension, and from the American Cancer Association for its work on mechanisms of cell growth.

3. Pharmaceutical/Industrial Collaborations

Increasing the revenue from industrial collaborations is a longterm goal; therefore, revenues from this initiative are not included in the five-year Strategic Plan. A task force should be established to acquire information on companies that may have long range goals or specific ongoing programs that mesh well with the goals and expertise of the Institute. This group should plan the initiation of contacts with the appropriate companies. The goals will be: (1) to initiate an "intimate relationship" with 1 or 2 major pharmaceutical firms, allowing them to have a "window" on evolving, state of the art, basic science in return for licensing rights; (2) to initiate individual scientific collaboration between Industry and the Institute that may result in sponsored research; (3) to obtain named sponsorship for seminar programs; (4) to establish Sabbatical/Internship Programs that will allow industrial scientists and Institute scientists to learn specialized technologies and perform collaborative studies.

A joint venture with the Beth Israel Hospital has led to the establishment of the Boston Collaborative Heart Failure Center, encompassing a number of specific collaborative "discovery" research projects aimed at the cure of heart failure, through patient testing and multi-center clinical trial coordination of new potential therapies and diagnostic tools. Significant corporate support for the Center is being actively recruited.

Long term contracts with pharmaceutical companies may be of considerable benefit in providing financial stability, intellectual input, and access to new experimental tools. However, because of concerns regarding academic freedom, co-existing NIH

regulations, and legal complications, considerable caution should be applied before entering into such ventures.

B. Development/Public Relations

There are basically 3 sources of revenue for charitable contributions to BBRI:

REVENUE SOURCES

Individuals
Foundations
Corporations

Programs need to be strengthened in individual and foundation giving, and the need to develop and implement a strategy of fundraising from corporations should be evaluated and moved forward. It is of critical importance that the fundraising programs related to these revenue sources be built up and strengthened so as to provide BBRI with a solid and consistent Annual Fund program.

The revenue goals, however, should also be placed within the reality of the "marketplace", i.e. should be comparable to those of other basic research organizations somewhat similar to BBRI, e.g. Worcester Foundation or Jackson Labs. The fundraising revenue goals for BBRI should be realistic and therefore achievable, so as to create a sense of accomplishment and confidence among the solicitors and donors. One way of reaching this objective is to focus the Annual Fund on projects or programs, with clearly defined goals in each area. Following are suggestions for giving programs.

GIVING PROGRAMS

INDIVIDUALS

Board
Direct Mail
Special Events
Planned Giving
Major Gifts

The most significant addition to the current individual giving program is the development and implementation of a major gifts or special gifts program. Initially we will identify 5-10 major gift prospects and, with the assistance of volunteers, begin cultivating them for a major gift to BBRI. As we now have the Peabody Challenge in place, the major giving program will be focused on raising the \$300,000 needed to meet the challenge and purchase the X-ray crystallography equipment.

CORPORATE

We are beginning to move forward with two facets of a corporate giving program: soliciting new corporate donors for BBRI through proposals (Boehringer Mannheim; Boston Scientific), and assessing the need for and development of a volunteer Corporate Committee.

FOUNDATIONS

We have, in the past, benefited from the generous support of local foundations. We should strive to maintain this support, while broadening our contacts to national foundations. The possibility of programmatic or individual support from national foundations such as the Howard Hughes Medical Institute, Kresge Foundation, Keck Foundation, etc., is underway and it is anticipated that several proposals will go to national foundations in the second half of the year. These foundations may be appropriate sources for major items of capital equipment to complement new programs or recruitments.

Looking forward to the long term Development focus, two needs of the Institute emerge that will require vigorous fundraising activity: increasing BBRI's endowment, and building new space for the Institute. As these cannot happen concurrently, strategic decisions need to be made as to the priority for future campaigns; however, it is essential that both are undertaken at some time in the future.

PUBLIC RELATIONS

Lack of communication with the general public appears to be a major impediment to soliciting charitable contributions to BBRI, and effort should be invested in improving the visibility of the work done at the Institute while making the importance of this work more understandable. Recognition of the longterm importance and value of investment in basic science requires considerable vision and sophistication on the part of BBRI supporters, and this challenge needs to be considered as the public relations activity moves forward. The focus of the Institute has been sharpened and the mission clarified without sacrificing the fundamental commitment to basic research; these objectives must be continued and strengthened. With the assistance of a public relations consultant, a solid, comprehensive foundation for increasing and improving BBRI's public relations efforts will be built and implemented. The three areas that the public relations activity will focus on strengthening and expanding are: 1: media relations; 2) communications/publications; and 3) government (federal, state, and local) liaison development.

Additionally, the visibility of the Institute can be raised by building bridges with the Harvard teaching hospitals and other area institutions, and by sponsoring high

quality symposia. With respect to clinical interactions, a work group is needed to outline the possibilities for interaction with clinical departments at Harvard hospitals. The combined expertise and interests could form the basis for a number of individual, high visibility collaborations as well as potential SCOR and Center grant applications. At the present time, opportunities appear to be greatest with regard to interactions with the Department of Medicine at the Beth Israel Hospital in Boston, where the new Director of the BBRI will continue to hold a Faculty position; however, possible collaborations with all Boston hospitals will be explored and considered.

Three specific initiatives will be considered: (1) An application for an NIH-funded training program to allow research-oriented clinical trainees at Boston-area hospitals to pursue 2-3 years of basic research training at the Institute. The cross-fertilization of expertise should be of interest to all parties involved; (2) the creation of a foundation (similar to Whitaker) to fund interactive projects between Boston-area hospitals and BBRI; members of both institution's governing boards will be invited to contribute, and peer review of grant applications will be performed by four individuals from the two institutions; (3) the Boston Collaborative Heart Failure Center.

In regards to symposia, an international symposium honoring the career of John Gergely will be held on July 27-29, 1996, and a second "Seidel Symposium" in the spring of 1997, continuing with a focus in the area of Muscle will be organized within the next two years and should become a regular event. Consideration should be given as to whether the focus should continue to be smooth muscle. Additionally, the idea of an event possibly co-sponsored by another research institute and the BBRI, possibly funded by a private foundation or covered by public broadcasting to investigate the future of basic biomedical research should be developed and, at the appropriate time, a work group should be formed to implement the project.

The BBRI public relations plan is composed of several strategies, each aimed at a very specific objective for the coming year. The foundation that should result from the development and implementation of these concurrent pieces will, hopefully, provide the base on which to continue to build in the future.

C. Investments

BBRI, through the collective efforts of its faculty and Development Office, has built up an investment portfolio of over \$7,000,000. The portfolio is managed by the Investment Committee, comprised of Trustees and senior management staff of the Institute.

The Investment Committee has established a set of investment goals within defined parameters. Currently, the portfolio consists of mutual funds ranging from money market to aggressive growth funds. Historically, 5% of the average portfolio balance for the prior three years is available for annual operations. In addition, it is

anticipated that, over the long run, investment income will be sufficient to pace the principal growth with inflation.

D. Technology Transfer

Since 1982, BBRI scientists initiated a number of projects that were funded by corporate research contracts, with the three major contracts bringing \$1.6 million in research funds to BBRI in the period 1982-1994. In addition, through the auspices of BBC, a solely-owned for-profit subsidiary of BBRI, Institute scientists have been awarded five phase I grants through NIH's Small Business Innovative Research (SBIR) program. Eight patents have been issued to BBRI, and one of these is just about to produce an income for BBRI from a licensing agreement.

No matter how impressive this record may be for an institute as small as BBRI, it was the result of sporadic initiatives by individual scientists and not the result of long-term planning. There is no question that a systematic technology transfer effort could have opened additional opportunities for corporate research and licensing agreements. In recognition of this important potential source of research funding and revenue, BBRI has recently become a member of the United Office of Technology Transfer of MBRI (Massachusetts Biotechnology Research Institute), which provides effective technology transfer services to a number of Boston area academic institutions.

In the past year, MBRI has conducted a detailed technology assessment of BBRI and has played an important educational role by increasing the awareness of BBRI scientists of technology transfer opportunities. This has set the stage for a systematic technology transfer effort, whose core will be the marketing of BBRI intellectual property to biotechnology companies, major pharmaceutical companies, and venture capital. An important component of this initiative will be to identify technology areas in which BBRI has particular strengths and market those as a package so as to enhance their impact and visibility. Another opportunity is offered by the SBIR funding mechanism, especially through the large phase II grants, which would require a reexamination of the role of BBC, including the possibility of joint ventures between BBC and established biotechnology companies. It is hoped that through aggressive efforts along these lines, research funding and licensing income from corporate sources will expand significantly above the current \$100,000 annual average.

III. Expenses

A. Directs

The responsibility of budgeting for and monitoring the expenditure of direct costs associated with a specific grant has traditionally been held by the Principal Investigator who submitted the grant. Such costs include salaries and fringe benefits, supplies, publication and travel related to a grant. BBRI has always maintained a

policy of conserving research funds and has been very successful, thanks to the efforts of the faculty, in limiting unnecessary spending of grant-related revenue.

This system of allocating and monitoring grant-related revenue is in keeping with BBRI's overall philosophy of encouraging independence and creativity among the faculty, and we feel strongly that this policy is a valuable incentive in the recruiting process.

B. Indirects

The Institute has been, and continues to be committed to keeping its administrative staffing levels lean and multi-functioning. In many cases this means foregoing individuals hired specifically to perform functions such as purchasing, research administration and equipment maintenance and scheduling. Instead, systems are designed in such a manner to provide these functions with existing personnel, e.g. the Director acts as both Chief Executive Officer while managing a full time laboratory; the Assistant Director is responsible for all physical plant management as well as financial matters; Principal Investigators assume the purchasing role as well as pursuing and expanding their research projects.

The indirect cost rate will be negotiated in early 1997 and will take effect September 1, 1997. This is an area of critical concern to the Institute. There is a clear justification for an increase of the indirect cost rate. However, the Department of Health and Human Services is under pressure to lower indirect cost rates. We have made an assumption in the budget that our indirect cost rate will be increase by 10% of its current rate (to approximately 96% of personnel costs).

Although we have hit a particularly trying time for annual funding, we have a solid financial base, are debt-free, and have a commitment of financial and managerial support from the Board of Trustees. We believe the influx of new talent, combined with the scientific goals established in this plan, will be the foundation for our continued success.

BOSTON BIOMEDICAL RESEARCH INSTITUTE

POLICIES AND PROCEDURES MANUAL

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TIME AND EFFORT REPORTING

Time and effort reporting is done on a pre-prepared listing which is distributed monthly by the Accounting Office.

There will be a page for each fund number showing the employees charged to the fund and the percentage of their salaries. This listing must be signed and dated by the Principal Investigator and returned to the Accounting Office.

Transfers, if required, will be posted to these sheets by the Accounting Office from signed Authorization for Transfer of Expenditure forms.

SICK AND VACATION TIME REPORTING

Support staff sick and vacation time is reported on a monthly basis. The Sick and Vacation Leave form is distributed by the administrative assistant. The completed form must be signed by the staff member and approved by the Principal Investigator, then returned to Accounting for centralized payroll record keeping.

FACULTY REAPPOINTMENT

Any Scientist, Principal Scientist, or Senior Scientist shall be notified one year before the term of his/her appointment expires whether the appointment will be recommended for renewal by the Committee on Research. Scientists who have received formal warnings that they may not be reappointed may be granted one-year extensions. The decision whether to give an extension will be made in a timely manner. If no formal warning is given, scientists are eligible for full term reappointments.

Amongst the criteria for considering reappointments are:

- Continued scientific productivity as evidenced by publications and grants.
- Service to the Institute.
- Scientific reputation.

Any Scientist, Principal Scientist, or Senior Scientist appointment not recommended for renewal shall be extended so as to provide one-half, one, or two years respectively, between the action and the expiration of the current appointment.

JOB DESCRIPTION

SCIENTIST

Scientists are appointed for three-year terms, Principal Scientists for four-year terms and Senior Scientists for five-year terms. These ranks correspond to the positions of Assistant Professor, Associate Professor, and Full Professor, respectively. Persons appointed to this category are classified as regular employees and may be on a full-time or part-time basis.

Qualifications:

The qualifications for an appointment are as follows:

Senior Scientist: established scientists of high standing internationally in their field as evidenced by at least two letters of recommendation by renowned colleagues.

Principal Scientist: should have repeatedly demonstrated the ability to compete successfully as a Principal Investigator for a research grant or equivalent productivity at the national level.

Scientist: usually has had at least three years of post-doctoral or equivalent experience prior to the appointment and is usually the Principal Investigator of a research project.

GRANTS BRIDGE SUPPORT FOR FACULTY

FIRST YEAR

- A first year of bridge support in an amount equal to the PI's salary is given to productive members of the faculty contingent upon timely submission of competitive grant applications.
- The amount of bridge support is proportional to the percentage of the PI's time allocated to the specific grant whose funding is delayed.
- If funding is received before bridge support runs out, unused moneys will be returned to the Institute.
- Application does not require submission of pink sheets and scores but does require a financial statement.
- For faculty members who have previously received bridge support, a new round of bridge support can only be obtained after successfully obtaining a full R01-type grant (e.g. NIH, NSF, SBIR) of three years or longer, or comparable supports.

SECOND YEAR

- Only available in exceptional circumstances, provided the Board of Trustees approves the request.
- PI must submit to the COR with the application for a second year of support:
 - Scores and pink sheets from most recent NIH review
 - CV
 - Letter outlining the PI's plan for successfully building his/her program and obtaining funding
- Criteria to be used in making decision of whether to recommend second year of bridge support:
 - Probability of funding
 - Excellence of science
 - Contributions to Institute
 - Programmatic fit

Boston Biomedical Research Institute**SPACE ALLOCATION PRINCIPLES AND GUIDELINES**

1. The Institute is committed to providing appropriate research space to every active and productive BBRI Investigator.
2. The Committee on Research functions as the Research Space Committee on behalf of all BBRI Investigators.
3. All space is collective BBRI space.
4. Space allocation decisions are made by the Committee on Research based on a consensus between the Director and a majority of the COR with input from the faculty member directly affected.
5. In the rare circumstance consensus cannot be met, the Director can request the appointment of a special joint committee of Trustees and non-COR members of the faculty for mediation.
6. All research space is subject to an annual review. When space is determined by the Committee on Research to be underutilized or utilized inefficiently, a reasonable amount of time will be provided to the Investigator for programmatic consolidation. Every reasonable effort will be made to accommodate the Investigator with contiguous space with a one bay minimum being allotted to funded Investigators.
7. Space is allocated to individual BBRI Voting Investigators.
8. Formal space requests are to be submitted to the Committee on Research in a timely manner in advance of the need for space.
9. Investigators shall notify the Committee on Research if allocated space can be reasonably consolidated or is no longer needed.
10. Space allocation is to be determined by fair and equitable guidelines, and these guidelines will be reviewed periodically, not less than once per year:

Space Allocation Guidelines are broken into two categories –

Formula Space Allocation (see below)

- Availability of appropriate space
- Demonstrated need for space
- External funding consistent with space
- Historic, current, and projected productivity

BOSTON BIOMEDICAL RESEARCH INSTITUTE

BY-LAWS

[as amended through November 15, 2001]

separate affirmative vote of the Trustees and Faculty, taken one year prior to the expiration of the Director's term.

The Deputy Director shall be appointed annually by and from the Faculty for a one-year term, upon recommendation of the Director.

Section 3. Assistant Officers. The Board of Trustees may appoint an Assistant Treasurer, an Assistant Secretary-Clerk and such administrative officers as it may from time to time believe necessary. Such additional officers need not be members of the Corporation. They shall serve from the time of their appointment until the first meeting of the Board following the next succeeding Annual Meeting.

Section 4. Vacancies. Any vacancy occurring in the office of any of the officers of the Corporation, except that of the Director and the Deputy Director, may be filled at any time by the Board of Trustees, and any person elected to fill such a vacancy shall hold office for the remainder of the term of the Officer whose place he/she takes. In the event of a vacancy in the office of Director, the Deputy Director shall assume the office until such time as the Trustees appoint an acting Director. If the Deputy Director shall resign or be or become unable to serve for the remainder of the term, the Director, after consultation with the Committee on Research, may appoint an interim Deputy Director who shall assume the office for the remainder of the term.

Section 5. Number of Offices Held. Except as otherwise specifically required by law or as otherwise specifically provided by these By-laws any person may hold two or more offices in the Corporation at the same time.

ARTICLE V

FACULTY

Section 1. Faculty. All Staff Scientists holding appointments for terms of not less than three (3) years shall constitute the Faculty. It shall from time to time advise the Committee on Research on matters relating to the scientific and educational activities of the Corporation, except as otherwise provided in these By-laws.

Section 2. Tenure.

A. The Board of Trustees may from time to time grant an appointment with tenure to a staff scientist at the Institute. Such appointments shall be made only on the recommendation of an ad hoc tenure committee to be appointed by the Board of Trustees, and with the approval of two-thirds of the members of the Committee on Research.

B. **Tenure, as such term is used in the By-laws, shall mean a permanent appointment to the staff of the Institute and a guarantee of the reasonable use of the research laboratories or other facilities of the Institute consistent with the research funding available to the staff member subject to the following conditions:**

1. Tenure shall terminate on retirement or upon resignation of the staff scientist or pursuant to revocation for grave misconduct or neglect of duty by a vote of two-thirds of the members of the Board of Trustees, upon the recommendation of the Committee on Research.
2. Tenure may be withdrawn by the Board of Trustees upon recommendation of two-thirds of the members of the Committee on Research if the research being conducted by that individual becomes inconsistent with the research program of the Institute.
3. Such further conditions as may be imposed by the Committee on Research in individual cases.
4. All determinations by the Board of Trustees hereunder shall be final and binding on all persons.

ARTICLE VI

DUTIES OF OFFICERS

Section 1. Chairman. The Chairman shall be the senior officer of the Corporation. He/she shall cause to be prepared the agenda of the Annual Meeting and of all special meetings of the Corporation in cooperation with the Director, and he/she shall preside at all meetings of the Corporation. In addition, he/she shall perform such other special duties as from time to time may be determined by the members of the Corporation.

Section 2. President. The President shall preside at the meetings of the Board of Trustees, and he/she shall cause to be prepared the agenda of the meetings of said Board in cooperation with the Director.

Section 3. Vice Presidents. The Vice Presidents shall assist the President in the performance of his/her duties and shall act for the President in the latter's absence.

Section 4. Director. The Director shall be the chief executive officer of the Corporation. He/she shall report to and carry out the general policies established by the Board of Trustees, which shall regularly review the performance of the Director. As chief executive officer he/she shall be responsible for the direction, management and implementation of the scientific and educational activities and policies of the Corporation consonant with the determinations of the Committee on Research with respect to all matters related to such activities. In addition, he/she shall perform such other duties and have such other powers as the Board of Trustees may from time to time determine. The Director shall preside at the meetings of the Committee on Research.

Section 5. Deputy Director. The Deputy Director shall assist the Director in the performance of his/her duties and in his/her absence shall act for the Director.

BOSTON BIOMEDICAL RESEARCH INSTITUTE

OFFICE OF THE EXECUTIVE DIRECTOR

20 STANFORD STREET, BOSTON, MASSACHUSETTS 02114
Area Code 617 • 742-2010

May 15, 1989

Victor A. Raso, Ph.D.
Department of Fine Structure

Dear Dr. Raso:

I am pleased to inform you that the Committee on Research has approved your appointment as Senior Scientist in the Department of Fine Structure. This appointment is for a five-year period, 4/1/89 through 3/31/94 and the salary arrangements are subject to the continuing availability of funds from sources outside the Institute.

Sincerely yours,



John Gergely, M.D., Ph.D.
Deputy Executive Director

JG/pb

cc: Dr. Davison

BOSTON BIOMEDICAL RESEARCH INSTITUTE

OFFICE OF THE EXECUTIVE DIRECTOR

20 STANIFORD STREET, BOSTON, MASSACHUSETTS 02114
Area Code 617 • 742-2010


March 22, 1988

Victor A. Raso, Ph.D.
Dept. of Fine Structure

Dear Dr. Raso:

I am pleased to inform you that the Committee on Research has approved your appointment as Visiting Scientist in the Department of Fine Structure. This appointment is for a one-year period, 2/1/88 through 1/31/89, and the salary arrangements are subject to the continuing availability of funds from sources outside the Institute.

Sincerely yours,



John Gergely, M.D., Ph.D.
Deputy Executive Director

JG/pb

cc: Dr. Davison

BOSTON BIOMEDICAL RESEARCH INSTITUTE

20 STANIFORD STREET, BOSTON, MASSACHUSETTS 02114
Area Code 617 • 742-2010
Telefax 617 • 523-6649

February 28, 1994

Victor A. Raso, Ph.D.
Senior Scientist

Dear Dr. Raso:

I am pleased to inform you that you have been reappointed as Senior Scientist. This appointment is for a five-year period, 4/1/94 through 3/31/99, and the salary arrangements are subject to the continuing availability of funds from sources outside the Institute and satisfactory performance of duties.

Sincerely yours,



John Gergely, M.D., Ph.D.
Director

JG/pb

NEW ISSUE

In the opinion of Ropes & Gray, Bond Counsel to the Institution, under existing law, interest on the Series 1999 Bonds is excluded from the gross income of the owners of the Series 1999 Bonds for federal income tax purposes, assuming continued compliance by the Issuer and the Institution with the Internal Revenue Code of 1986, as amended. Interest on the Series 1999 Bonds is not an item of tax preference for purposes of the federal alternative minimum tax imposed on individuals and corporations. However, interest on the Series 1999 Bonds will be taken into account in determining adjusted current earnings for the purpose of computing the alternative minimum tax imposed on certain corporations (as defined for federal tax purposes). In the opinion of Bond Counsel to the Institution, under existing law, the Series 1999 Bonds and any income derived therefrom, including any income from any sale, exchange or transfer of the Series 1999 Bonds, shall at all times be free from Massachusetts taxation, although the Series 1999 Bonds and the interest thereon are included in the measure of Massachusetts estate and inheritance taxes and of applicable Massachusetts corporation excise and franchise taxes. For federal and Massachusetts tax purposes, interest includes original issue discount. See "TAX EXEMPTION" herein.

\$17,000,000

MASSACHUSETTS DEVELOPMENT FINANCE AGENCY

Revenue Bonds

(Boston Biomedical Research Institute, Inc. Issue - Series 1999)

Dated: February 1, 1999

Due: February 1, as shown below

The Massachusetts Development Finance Agency Revenue Bonds (Boston Biomedical Research Institute, Inc. Issue - Series 1999) (the "Series 1999 Bonds") are issuable only as fully registered bonds without coupons and, when issued, will be registered in the name of Cede & Co., as Bondowner and nominee for The Depository Trust Company ("DTC"), New York, New York. DTC or its custodial agent will act as securities depository for the Series 1999 Bonds. Purchases of the Series 1999 Bonds will be made in book-entry form, in the denomination of \$5,000 each or any integral multiple thereof. Purchasers will not receive certificates representing their interest in Series 1999 Bonds purchased. So long as Cede & Co. is the Bondowner, as nominee of DTC, references herein to the Bondowners or registered owners shall mean Cede & Co., and shall not mean the Beneficial Owners (as hereinafter defined) of the Series 1999 Bonds.

Principal and semiannual interest on the Series 1999 Bonds will be paid by State Street Bank and Trust Company, as trustee (the "Trustee") and paying agent. So long as DTC or its nominee, Cede & Co., is the Bondowner, such payment will be made directly to DTC. Disbursement of such payments to the DTC Participants is the responsibility of DTC and disbursements of such payments to the Beneficial Owners is the responsibility of the DTC Participants, all as more fully described herein. Interest will be payable on August 1, 1999 and semiannually thereafter on February 1 and August 1 to the Bondowners of record as of the close of business on the fifteenth day of the month preceding such interest payment date.

The Series 1999 Bonds shall be special obligations of the Massachusetts Development Finance Agency (the "Issuer") doing business as "Mass Development".



MASSDEVELOPMENT

The Series 1999 Bonds will be issued pursuant to a Loan and Trust Agreement dated as of February 1, 1999 (the "Agreement") among the Issuer, Boston Biomedical Research Institute, Inc., (the "Institution") and the Trustee. The Issuer will loan the proceeds of the Series 1999 Bonds to the Institution. The Series 1999 Bonds are payable solely from and secured by payments to be made to the Trustee for the account of the Issuer by the Institution and from such other funds as may be available therefor under the Agreement. Reference is hereby made to this Official Statement for pertinent security provisions of the Series 1999 Bonds.

THE SERIES 1999 BONDS DO NOT CONSTITUTE A GENERAL OBLIGATION OF THE ISSUER OR A DEBT OR PLEDGE OF THE FAITH AND CREDIT OF THE ISSUER OR A DEBT OR PLEDGE OF THE FAITH AND CREDIT OF THE COMMONWEALTH OF MASSACHUSETTS OR ANY POLITICAL SUBDIVISION THEREOF; EXCEPT TO THE EXTENT PAID FROM BOND PROCEEDS, THE PRINCIPAL OF, PREMIUM, IF ANY, AND INTEREST ON THE SERIES 1999 BONDS ARE PAYABLE SOLELY FROM THE REVENUES AND FUNDS PLEDGED FOR THEIR PAYMENT IN ACCORDANCE WITH THE AGREEMENT. THE ISSUER HAS NO TAXING POWER.

MATURITIES, AMOUNTS, RATES, AND PRICES OR YIELDS

Due February 1	Principal Amount	Interest Rate	Price or Yield	Due February 1	Principal Amount	Interest Rate	Price or Yield
2001	\$255,000	5.00%	4.25%	2006	\$330,000	5.00%	4.85%
2002	270,000	5.00	4.45	2007	345,000	5.00	4.95
2003	285,000	5.00	4.60	2008	360,000	5.00	100
2004	295,000	5.00	4.70	2009	380,000	5.10	100
2005	310,000	5.00	4.75				

\$5,170,000 5.65% Term Bonds Due February 1, 2019 to yield 5.68%
\$9,000,000 5.75% Term Bonds Due February 1, 2029 - Price 100%
(Accrued interest to be added from February 1, 1999)

THE SERIES 1999 BONDS ARE SUBJECT TO REDEMPTION PRIOR TO MATURITY AT VARIOUS PREMIUMS, OR AT PAR UNDER CERTAIN CIRCUMSTANCES, AS MORE FULLY SET FORTH HEREIN.

The Series 1999 Bonds will be offered, when, as and if issued and accepted by the Underwriter, subject to prior sale, to withdrawal or modification of the offer without notice, and opinions as to legality and certain other matters by Ropes & Gray, Boston, Massachusetts, Bond Counsel to the Institution. Certain legal matters will be passed upon for the Institution by its counsel, Ropes & Gray, Boston, Massachusetts. Certain legal matters will be passed upon for the Underwriter by its counsel, Edwards & Angell, LLP, Boston, Massachusetts. The Series 1999 Bonds are expected to be available for delivery to DTC in New York, New York, or its custodial agent, on or about February 19, 1999.

State Street Bank and Trust Company

February 11, 1999

Management's Discussion of Recent Financial Performance

Operations. The Institute has achieved operating gains and an excess of total unrestricted expenses in 27 of the last 29 years. The following table shows the operating performance operating revenue for BBRI over the past five years.

Operating Performance

	1994	1995	1996	1997	
Increase (decrease) in unrestricted net assets	\$539,168	\$732,669	(\$643,726)	\$1,687,901	
Unrestricted support	\$7,207,143	\$7,446,777	\$6,092,687	\$6,850,500	
Operating Margin	7.5%	9.8%	(10.6%)	24.6%	10.6%

Approximately 90% of BBRI's grant revenue generates from funding by the NIH. Revenues from grants and contracts has decreased from a peak of \$6,956,725 in 1994 to \$5,164,438 in 1998. The lower level of grant revenues in year 1997 and 1998 is a result of the slowdown in new grant applications and approvals that occurred in 1995 during the appointment of the new Director. Management also attributes this decline to the combination of recruitment time of new scientists coupled with the NIH's lengthy grant application and approval process. All grants issued by the NIH are awarded after an intensive competitive grant application process. Assuming approval, the grant is funded nine months from the application date. In addition, in 1995, BBRI developed a strategic recruitment plan to hire two new principal investigators per year. This recruitment plan coincided with the expiration of several grants and the appointment of the new Director.

Management anticipated the decline in grant revenues in 1996 and 1997, and opted to position itself for future expansion. BBRI let go several investigators that did not have grant funding and started a new recruitment program. BBRI successfully recruited two new investigators in August and September 1995, and supported their research activities until they received grant funding in May and March, 1996, respectively. In addition BBRI retained several investigators whose grant funding was interrupted but whom BBRI felt were likely to regain funding. This strategic decision led to an operating loss in 1996, but management believes it has strengthened the Institute moving forward.

Since 1996, BBRI has recruited six additional investigators, three of whom have received funding, two of whom are awaiting decisions on grant applications, and the remaining investigator joined the BBRI faculty in the January, 1999. In 1997, BBRI moved several of its investigators into non-salaried positions reflecting their grant funding status.

For the five month period ending November 30, 1998 compared with five months ending November 30, 1997, grant revenue increased 6.9% while salaries and benefits only increased 6.0%. During the same period, BBRI experienced an investment income loss of \$102,912. This loss is primarily related to a downturn in the stock market during this period and consists of \$340,770 of unrealized losses and \$237,858 of realized gains, dividends and interest. During this five month period, BBRI received eight new grant awards. Four of these grants are expected to increase BBRI's revenue in the second half of 1999.

The NIH grants range from three to five years with the targeted goal of NIH to have the average grant length of four years. This grant length provides stability for the Institute and creates a revenue backlog. The current backlog of grants approved for funding for the Institute was \$17.5 million (as of June 30, 1998) and is expected to increase. Since June 30, 1998 the Institute has received eight additional new grants approved totaling \$5,607,337. Management fully anticipates grant revenue to return to and exceed 1994 results by the year 2000. The 1999 budget projects an increase in grant revenues of 20% to \$6.27 million.

BOSTON BIOMEDICAL RESEARCH INSTITUTE

Victor A. Raso, Ph.D.

20 STANFORD STREET, BOSTON, MASSACHUSETTS 02114
Area code 617 • 742-2010
Telefax 617 • 523-6649

November 21, 1996

To The Members of The Committee On Research:

At the end of November funds will run out on a 6-month Small Business Innovation Research Grant "Catalytic Antibodies for the Treatment of AIDS." This money (99,911 - 38,174 BBRI service fee) has been sustaining my laboratory following the finish of institutional support. Unfortunately, it now appears that the re-submitted competing continuation of my NIH grant "Targeting Toxins with Acid-Triggered Hybrid Antibodies" will not be funded this round. I am therefore writing to request institutional funds for second year support to temporarily operate the laboratory (one year salary plus supplies) while NIH and other funding is being sought.

The prospects for future support are as follows:

1. Experiments are underway to obtain data for second phase funding of the recently awarded 6-month Small Business Innovation Research Grant "Catalytic Antibodies for the Treatment of AIDS".
2. A similar NIH R01 grant "Catalytic Antibodies Directed Against HIV" will also be submitted.
3. My NIH grant "Targeting Toxins with Acid-Triggered Hybrid Antibodies" will either be re-submitted for competing renewal or more-likely will be revised as a new grant "Targeting Binary Toxins" to better reflect its renovated scientific direction.
4. A new NIH grant "Amyloid β -Peptide Equilibria in Alzheimer's Mice" is currently being written. ✓
5. A related grant, "Catalytic Antibodies for the Treatment of Alzheimer's Disease" will be submitted as an SBIR grant and also to the Alzheimer's Association. ✓

Given the scope and relevance of the topics addressed, I believe that at least one of these grants will be funded.

To help strengthen the competing renewal grant application, I have submitted two manuscripts that are currently being reviewed by the *Journal of Biological Chemistry*.

I believe that I have made a positive contribution to the BBRI over the years and with eventual funding hope to do so in the future. While the "fit" of my research may not be ideal in the current scheme of things, it has always been on the cutting edge of biomedical research and has excited interest among our non-scientist supporters.

With regard to personnel, Christine Kearney is currently providing essential technical assistance on the AIDS, cancer therapy and Alzheimer's disease projects in addition to maintaining the smooth operation of all laboratory support functions. I will utilize my salary to keep Christine working at the BBRI.

Sincerely,

A handwritten signature in dark ink, appearing to read "Vic Raso", with a long, sweeping horizontal stroke extending to the right.

Vic Raso, Ph.D.

November 21, 1996

BRIDGE SUPPORT

FIRST YEAR

- A first year of bridge support in an amount equal to the PI's salary is given to productive members of the faculty contingent upon timely submission of competitive grant applications.
- The amount of bridge support is proportional to the percentage of the PI's time allocated to the specific grant whose funding is delayed.
- If funding is received before bridge support runs out, unused moneys will be returned to the Institute.
- New faculty are required to have used all of their seed money before being eligible to request bridge funding and to have successfully brought in a grant submitted from the BBRI in order to be eligible.
- Application does not require submission of pink sheets and scores but does require a financial statement.
- For faculty members who have previously received bridge support, a new round of bridge support can only be obtained after successfully obtaining a full RO1-type grant (e.g. NIH, NSF, SBIR) of three years or longer, or comparable support.

SECOND YEAR

- Only available in exceptional circumstances until additional sources of revenue are available to the Institute.
- PI must submit to the COR with the application for a second year of support:
 - Scores and pink sheets from most recent NIH review
 - CV
 - Letter outlining the PI's plan for successfully building his/her program and obtaining funding
- Criteria to be used in making decision of whether to recommend second year of bridge support:
 - Probability of funding
 - Excellence of science
 - Contributions to Institute
 - Programmatic fit

Kill's new policy

BOSTON BIOMEDICAL RESEARCH INSTITUTE

COMMITTEE ON RESEARCH

November 27, 1996

A regular meeting of the Committee on Research was held on Wednesday, November ²⁷~~28~~, 1996, at 10:00 a.m. Present at the meeting were Drs. Morgan, Grabarek, Paulus, Raso, and Wang. Others present were Mr. Thomas McQuaid, and Ms. Barbara Zillman, who recorded the proceedings.

1. Dr. Morgan asked for approval of the minutes of October 29, 1996. Clarification was requested on three items. They were as follows:

1) In item 5, concerning Dr. Volloch, the term "bridge support" is inaccurate and should be redefined as "R21 support." 2) Same sentence, the term "scientific misconduct" is inaccurate and should be restated as "alleged misconduct...." 3) In item 6, concerning potential BBRI floor space, the discussion is more accurately reflected with the following addition after the phrase ".....room itself belongs to BBRI.": "Dr. Grabarek asked if the room is available immediately and Mr. McQuaid replied that it is not."

With these clarifications noted, it was

VOTED: Unanimously, to approve the minutes of October 29, 1996.

Following this vote, Dr. Morgan recapped for the record, because of subsequent events, the intent of the C.O.R., at its last meeting, to provide Dr. Volloch with temporary laboratory space following his relocation from the second floor. Dr. Leavis had volunteered to clear one and one-half of his own benches for use by Dr. Volloch, with the understanding that if Dr. Leavis was awarded his then-pending grant application, his space would be returned. Dr. Leavis has since learned that his grant application has been awarded and he will need to reclaim his lab for expansion of his program. The ESR room in the basement was made available, temporarily, to Dr. Volloch by Dr. Graceffa. Dr. Graceffa and Dr. Gergely are composing a letter to Dr. Volloch stating that he is to vacate the ESR room by a specified date and that while occupying it, there are not to be radioactives used in that room, and that the equipment must not be harmed. C.O.R. members agreed with the appropriateness of giving Dr. Volloch such a letter. The following issues were reiterated: the allocation of space in the basement to Dr. Volloch is temporary; the C.O.R. as a body, and each member individually, must work to see that Dr. Volloch submits a follow-up competitive renewal grant application to the NIH - the conditions of the R21 that Dr. Volloch received require this and assure expedited review if he submits his application on time; the C.O.R. must consider upon submission of that grant application, what to do next. The decision concerning his application should be known in July. If triaged, Dr. Volloch will be asked to leave the Institute but if funded, he may be allowed to stay. Funding must be from the NIH; an Alzheimer's grant would not be enough. If asked to leave, he is to be given advance notice (if outcome is in July, notification would be for relocation in September). In any case, he has been made no promise as to continued lab or office space beyond his current funding. If during his accelerated review, his score is in the top 30%, he will be allowed to resubmit his application for the summer deadline.

2. The next item of discussion was setting a policy on misconduct proceedings. There was some discussion about this topic and it was agreed to continue without formal policy implementation.

3. Proposals were discussed next. The first was that of Dr. Coleman.

Dr. Coleman has made a request for his first year of bridge support (see attached). Using the current guidelines for granting requests for bridge support, Dr. Coleman was evaluated on several items and concerns were raised by C.O.R. members. Dr. Grabarek noted that Dr. Coleman has not been active in publishing since 1994. Dr. Paulus noted that Dr. Coleman had been appointed to a faculty position at the Institute with two active NIH grants, and never re-applied for the grants when they

expired. Further, he has made himself very part-time at the Institute. A formal vote by the C.O.R. in October, 1991 guaranteed him a salary for three years, contingent upon his funding. Dr. Coleman now has no funding. C.O.R. members concluded that by current guidelines as well as the vote of the C.O.R. in October, 1991, Dr. Coleman does not qualify for full bridge support. Some further discussion took place and it was moved, and by a majority,

VOTED: Because of questions of productivity and failure to renew grant applications in a timely fashion, but because of past contributions to the Institute, three months salary support will be awarded to Dr. Coleman, using his base salary of \$70,000. This is consistent with the determination of the October 2, 1991 meeting of the C.O.R.


There were four aye votes and one ~~may~~ ^{abstention by Dr. Vaso} vote.

The second proposal to be discussed was that of Dr. Raso. He left the room while discussions took place.

Dr. Raso is requesting his second year of bridge support (see attached). His first year of support was awarded before the current criteria were established and his first year of support was very generous. The merits of Dr. Raso's proposal were deemed to be that he had brought in over a \$1,000,000 in overhead to the Institute. Furthermore, Dr. Raso has viable patents and is very technology-oriented, a future direction the Institute will take, and a probable revenue stream. The negative aspects of the proposal were considered to be a lack of publications. The amount to be requested was further refined by again referring to current criteria. Dr. Raso has already received an equivalent of 16 months of support, including supplies, in his first year of support. Therefore, a financial commitment of eight months will be made to him. It was,

VOTED: Unanimously, to request a second year of bridge support for Dr. Raso from the Board in an amount equivalent to eight months of both salary and supplies (at \$10,000 per year), and to allow that amount to be awarded effective immediately. This vote is subject to ~~reversal~~ ^{approval} by the Board at its next meeting in January, 1997.

4. There being no Other Business, the meeting was adjourned at 1:35 p.m.



Barbara Zillman

December 9, 1996

3 Step

BOSTON BIOMEDICAL RESEARCH INSTITUTE
AUTHORIZATION FOR PAYMENT TO PERSONNEL

*pay for his salary
by cutting his
own salary*

Salary ☒ Fellowship or traineeship ☐

NAME CHRISTINE KEARNEY POSITION RESEARCH ASSISTANT

STEP 21 ANNUAL SALARY 26,315 HR MANAGER JB
APPROVAL

Please check appropriate box: New employment ☐ Change in fund ☐
Change in salary ☒ Change in employment status ☐

Effective date: 1/1/97 Employment status: Permanent ☐ Temporary ☒ Full time ☒ Part Time ☐

Time slips ☐

Month	% Time	Fund No.	P.I. Approval
JANUARY	100	178	<i>Vic Kato</i>
FEBRUARY			
MARCH			
APRIL			
MAY			
JUNE			
JULY			
AUGUST			
SEPTEMBER			
OCTOBER			
NOVEMBER			
DECEMBER			

FOR ADMINISTRATIVE USE ONLY

Employee *JB*

Amount (use only one)

Monthly

Semi-Monthly *1096*

VISA type (if applicable)

Payroll category:

☒ 0 - Regular employee - all taxes withheld

1 - Fellow or Trainee - no FICA; no benefit % to grant

2 - Research fellow or trainee - benefit % to grant

5 - Exchange visitor - J-1 visa; F-1 visa and any others that do not require FICA withholding.

Married ☐

Single ☒

Withholdings: Federal 0 State 0 Exempt

Approved by: *Kato* Date Director Deputy Director

Effective date 4/1/96

I am recommending Christine Kearney for a three step merit increase because of her truly excellent performance at the Boston Biomedical Research Institute as a Research Assistant I. Christine joined my laboratory directly after graduating and had minimal experience doing actual scientific research on a professional level. Despite this she has independently maintained the smooth operation of all of the support functions which allow the laboratory to run effectively. Her ability to take over has been particularly important at a time when I have been increasingly pulled away from the laboratory to write grants and papers. In fact she generated some of the data presented in the HIV grant proposal and most of the preliminary data included in the new Alzheimer's disease grant is a direct result of her work. I will not attempt to list all of the technical skills which Christine has mastered but they range from mass spectral analysis to performing hybridoma fusions to generate the numerous monoclonal antibodies that we require for the research.



GLEEN G. MORGAN, Ph.D.
DIRECTOR

42-2010
27-6053 FAX
E: morgan@bbri.cri.harvard.edu



September 24, 1997

Victor A. Raso, Ph.D.
Senior Scientist
Boston Biomedical Research Institute
20 Staniford Street
Boston, MA 02114

Dear Vic:

As you know, your current appointment as a senior scientist at the BBRI extends for another two years. The Institute, however, does have a policy of reviewing appointments for senior scientists two years in advance, to provide warning if there is any possibility that the appointment may not be renewed. At this point I am writing to give you such warning. Given your current string of bad luck at the NIH, it may possibly be necessary for us to vote against renewal of your appointment two years from this date.

I was very pleased to discover today that you had recently succeeded in publishing two new papers in JBC. Congratulations! This should help you in your grant applications and it's my hope that successful funding of NIH or other similar grants will allow us to renew your appointment when the time comes.

You should be aware that the allocation of space is separate from the academic appointment but is also linked to the availability of funds for utilization of lab space. I hope that you will be willing to share any hint of good news with us as soon as you receive word on your grants.

Sincerely yours,

Kathleen G. Morgan, Ph.D.
for the Committee on Research

KGM/mfd

a/mtgs.../cor.raso

20 STANIFORD STREET, BOSTON, MA 02114

TERMINATION REPORT

NAME Victor A. Raso

SOC. SECURITY # 050-36-7225

SUPERVISOR Dr. Kathleen G. Morgan

POSITION Sr. Scientist

TERMINATION DATE 1/31/98

DATE OF HIRE 2/1/88

VACATION DAYS None

REASON FOR TERMINATION:
RESIGNED

DISCHARGED

☐ Accept Another Job

☐ Unsatisfactory Work Performance

☐ Other (Explain under Comments)

☐ Excessive Tardiness/Absenteeism

☒ Laid Off*

*Laid off means due to lack of work or funds, or job discontinued, etc.

COMMENTS:

Lack of funds

(Date) _____ (Supervisor's Signature) _____

(Date) _____ (Director's Signature) _____

IF YOU DISAGREE WITH ANY OF THE ABOVE, PLEASE NOTE HERE:

Date: _____ Employee's Signature _____

I do ____ do not ____ wish to continue my medical coverage. I understand that if I elect to continue this coverage I am responsible for the full cost, and that I will make monthly payments in advance to BBRI. If payments are not received by the due date, coverage will be terminated, except for the initial payment, which is due within 45 days.

I also understand that if I elect not to continue the coverage I can notify you in writing within 60 days from today or termination, whichever is later, that I do not want the coverage.

Date: _____ Employee's Signature _____

BOSTON BIOMEDICAL RESEARCH INSTITUTE

PATRICIA BROUILLETTE
HUMAN RESOURCES MANAGER

3078

MEMORANDUM

TO: Ginny Cahill
Accounting

FROM: Pat *Pat*

DATE: January 28, 1998

SUBJECT: Victor A. Raso, Ph.D.

This is to inform you that Victor A. Raso terminated his employment
at BBRI on December 31, 1998.

As soon as a termination report is completed I will send you a copy.

Reinstated 4/1/99 \$109,150.

Date: Fri, 10 Apr 1998 12:54:18 +0100

To: Raso

From: Kathleen Morgan <morgan@bbri.harvard.edu>

Cc: mcquaid@bbri.harvard.edu (Thomas J. McQuaid)

Vic--Just so there is no mis-communication. . . I wanted to confirm our discussion from earlier in the week. Since your SBIR will only run 6 months, doesn't really cover overhead and there's no sign of an RO-1 coming in in the foreseeable future, I will need to be bringing search candidates through your space, indicating that the space will be available for new faculty members.

However, we can make some space available for you in the basement and there is no need to move until the end of June. Of course, if you get a fundable score on one of your pending application in the June study sections--or any other possible source of support, please let me know ASAP.

Keeping my fingers crossed.
Kathy

NIAID > Funding > Grants and Contracts > All About
Grants > How to Write a Grant Application >
Before You Start Writing



tutorial index · next >>

Before you start writing your application, do some planning. It generally takes three to six months to write a grant application, and another nine months or so from the time you send it in till you get funded. Check with your institution's business office to see what deadlines it has -- you'll need to get the business official's signature before you send your application to NIH. Allow time for your own internal review and time to make the edits from it.



Next find out what documentation you'll need to prepare -- any special requirements, e.g., research animals or human subjects. See Define the Documentation You'll Need for more information, including details on submitting a data sharing plan and a plan for sharing model organisms.

One way to make sure your planning and feedback are adequate is to put together your own review committee before you write your application. Ask a few senior colleagues to be on it, and share your ideas with them while you're still in the concept stage. After you've agreed on a project, draft a short description of your specific aims and discuss these with the committee. This strategy will give you input early on and help you make sure you're writing and organizing effectively. And be sure to have the committee review the application after you're finished writing.

For tips for new investigators, go to Advice for New Investigators.

Additional Resources

- PHS 398 Application Form
- Laws Relevant to NIH
- Preparation Timeline
- Receipt to Review Timeline

- When to Contact an NIAID Program Officer
- CRISP database of biomedical research projects funded by the U.S. Public Health Service
- Before You Begin checklist
- Documentation checklist
- Previous tutorials, Grant Application Basics and How to Plan a Grant Application
- Next tutorial, How to Manage Your Grant Award
- Other tutorials available on our All About Grants page
- Data Sharing Policy SOP
- Sharing Model Organisms SOP

tutorial index · next >>



Department of
Health and
Human
Services



National
Institutes
of Health



National Institute
of Allergy and
Infectious
Diseases

October
6, 2004
(blh)



Date	Activity	Ref. No.
Tuesday, November 25, 1997	Prepared Alz-NH ₂ Frozen Stocks, 2 vials each of 3D9(H) & 3D9 (C).	B001564
Wednesday, November 26, 1996		
Thursday, November 27, 1997		
Friday, November 28, 1997		
Saturday, November 29, 1997	Weekend	
Sunday, November 30, 1997	Weekend	
Monday, December 1, 1997		
Tuesday, December 2, 1997		
Wednesday, December 3, 1997		
Thursday, December 4, 1997	Conducted radioactive experiment.	
Friday, December 5, 1997		
Saturday, December 6, 1997	Weekend	
Sunday, December 7, 1997	Weekend	
Monday, December 8, 1997	Analyzed capillary depletion data.	B001941
Tuesday, December 9, 1997		
Wednesday, December 10, 1997	Received radioisotope (¹²⁵ I; 10 mCi); Analyzed data: capillary depletion experiment (#2).	B001941 B001991-92
Thursday, December 11, 1997	Prepared grant application (SBIR): "Cerebral Antibody delivery...".	B00269A
Friday, December 12, 1997		
Saturday, December 13, 1997	Weekend; Analyzed and edited β -Amyloid peptide sequences.	B001941 B001989-90
Sunday, December 14, 1997	Weekend	
Monday, December 15, 1997		
Tuesday, December 16, 1997		
Wednesday, December 17, 1997		
Thursday, December 18, 1997		
Friday, December 19, 1997	Acquired digital images: various exposures.	B001969-88 B001844 B001940-41
Saturday, December 20, 1997	Weekend; Conducted radioactive experiment.	
Sunday, December 21, 1997	Weekend	
Monday, December 22, 1997	Analyzed images and data for mouse and 7D3/1G1.	B001844
Tuesday, December 23, 1997	Continued longer exposure; Analyzed data.	B001844
Wednesday, December 24, 1997	Holiday	
Thursday, December 25, 1997	Holiday	
Friday, December 26, 1997		
Saturday, December 27, 1997	Weekend	
Sunday, December 28, 1997	Weekend	
Monday, December 29, 1997		

Tuesday, December 30, 1997	Carried out immunofluorescent labeling; analyzed images [Preparation time 2-3 weeks.]	B001940 B001967-68
Wednesday, December 31, 1997	Holiday; Recorded required inventory of radioisotopes (31 st).	
Thursday, January 1, 1998	Holiday	
Friday, January 2, 1998		
Saturday, January 3, 1998	Weekend	
Sunday, January 4, 1998	Weekend	
Monday, January 5, 1998	Completed and signed "Intent to apply" for Grant "Cerebral Delivery of Vectorized..."	
Tuesday, January 6, 1998		
Wednesday, January 7, 1998		
Thursday, January 8, 1998		
Friday, January 9, 1998	Conducted radioactive experiment.	
Saturday, January 10, 1998	Weekend; Analyzed images: R17/5A11 – time course study.	B001842 B001940 B001966
Sunday, January 11, 1998	Weekend; Continued for longer exposures.	B001842
Monday, January 12, 1998	Continued for longer exposures.	B001842
Tuesday, January 13, 1998	Conducted radioactive experiment; Continued for longer exposures.	B001842
Wednesday, January 14, 1998	Continued for longer exposures.	B001842
Thursday, January 15, 1998	Ordered radioisotope (¹²⁵ I; 10 mCi); Continued for longer exposures.	B001842
Friday, January 16, 1998	Carried out Westernblot experiment; Analyzed data: R17/5A11.	B001842
Saturday, January 17, 1998	Weekend; Analyze data; continued for longer exposures; generated composites.	B001956-65 B001842 B001940
Sunday, January 18, 1998	Weekend; Compiled results from R17/5A11.	B001940 B001953-55
Monday, January 19, 1998	Holiday	
Tuesday, January 20, 1998	Continued Western blot experiment; Analyzed data: R17/5A11.	B001842
Wednesday, January 21, 1998	Revised and updated Alz. Vector file.	B001844
Thursday, January 22, 1998		
Friday, January 23, 1998	Analyzed data.	B001842
Saturday, January 24, 1998	Weekend; Analyzed data; Continued for longer exposures.	B001842
Sunday, January 25, 1998	Weekend; Analyzed data; Continued for longer exposures.	B001842
Monday, January 26, 1998	Completed and signed grant	B000270

	application form (PHS 398): "Cerebral Delivery..."; Analyzed data; Continued for longer exposures; CK sick.	B001842
Tuesday, January 27, 1998	Prepared standard with regression; generated standard curve.	B001842
Wednesday, January 28, 1998	Analyzed data; Continued for longer exposures; Acquired gel image: R17/5A11, 7D3/1G7.	B001842
Thursday, January 29, 1998	Analyzed data: 17/5A11, 7D3/1G7.	B001840
Friday, January 30, 1998	[Recorded monthly radioactivity (¹²⁵ I) disposal.*]	
Saturday, January 31, 1998	Weekend	
Sunday, February 1, 1998	Weekend	
Monday, February 2, 1998	Analyzed data: Alz.1-40/Tween, various exposures.	B001840
Tuesday, February 3, 1998	Continued longer exposures.	B001840
Wednesday, February 4, 1998	Continued longer exposures; Conducted Western blot experiment: R17/5A11.	B001840
Thursday, February 5, 1998		
Friday, February 6, 1998		
Saturday, February 7, 1998	Weekend; Prepared figures for vectorized anti-β-Amyloid imaging.	B001940 B001949-52
Sunday, February 8, 1998	Weekend	
Monday, February 9, 1998		
Tuesday, February 10, 1998		
Wednesday, February 11, 1998		
Thursday, February 12, 1998		
Friday, February 13, 1998	Conducted Retarding Gel experiment.	B001840
Saturday, February 14, 1998	Weekend; Continued longer exposures.	B001840
Sunday, February 15, 1998	Weekend; [A1-40 on polyamide??]	B001840
Monday, February 16, 1998	Holiday; Tested Alz.1-40 + 5A11 at various conditions; Analyzed data; Edited peptide sequences (Alz. 1-20; 21-40).	B001840 B001940 B001947-48
Tuesday, February 17, 1998	Tested Alz.1-40, PBS, + 5A11/7D3 at various conditions; analyzed data.	B001840
Wednesday, February 18, 1998	Compared different solvents for Alz.1-40; Analyzed data.	B001840
Thursday, February 19, 1998	Compared different proteases for Alz.1-40; Analyzed data.	B001840
Friday, February 20, 1998	Tested more conditions; analyzed data.	B001840
Saturday, February 21, 1998	Weekend	

Sunday, February 22, 1998	Weekend; Conducted radioactive experiment; Analyzed data: A14-25 CY.	B001840
Monday, February 23, 1998	Tested more different conditions; analyzed data.	B001840 B001566 B001567
Tuesday, February 24, 1998		
Wednesday, February 25, 1998	Requested animal usage protocol amendment for injection of Tg2576 mice; Analyzed data: R17/5A11 IP(-) Tg mice, two exposure durations.	B001748 B001840
Thursday, February 26, 1998	Set up breeding pair; continued with longer exposures for data/image.	B001772; B001769 B001760-62 B001840
Friday, February 27, 1998	Prepared liquid nitrogen frozen cell stocks for early hybridoma (anti-Alz.); analyzed data.	B001565 B001840
Saturday, February 28, 1998	Weekend; [Recorded monthly radioactivity (¹²⁵ I) disposal.*]	
Sunday, March 1, 1998	Weekend	
Monday, March 2, 1998	Prepared liquid nitrogen frozen stocks of human umbilical cord cells and human embryonic kidney cells (adenovirus); Acquired and analyzed image at 120 hours 20 minutes post-injection: R17/5A11 IP(-) Tg mice.	B001840
Tuesday, March 3, 1998		B001838
Wednesday, March 4, 1998	Analyzed data; acquired image: R17/5A11 (+) mice; analyzed image at 6 hours 20 minutes post-injection.	B001838
Thursday, March 5, 1998	Acquired and analyzed image at 24 hours 20 minutes post-injection.	B001838
Friday, March 6, 1998	Acquired and analyzed image at 48 hours 20 minutes post-injection.	B001838
Saturday, March 7, 1998	Weekend	
Sunday, March 8, 1998	Weekend	
Monday, March 9, 1998		
Tuesday, March 10, 1998	Analyzed images/data from various time points: R17/5A11 IP(-) Tg mice.	B001838
Wednesday, March 11, 1998	Filed animal protocol annual update form for "Productin of monoclonal antibodies for treating...";	B001751

	Analyzed data for A1-40/Tween IP(-) Tg mice.	
Thursday, March 12, 1998	Analyzed data for A1-40/Tween IP (+) Tg mice.	B001838 B001940
Friday, March 13, 1998	Continued IP experiments with various time points.	B001838
Saturday, March 14, 1998	Weekend; Continued IP experiments with various time points.	
Sunday, March 15, 1998	Weekend	
Monday, March 16, 1998	Conducted radioactive experiment; CK day off; Requested peptide synthesis (Alz. 17mer); Analyzed data for A14-25 (at pH7).	B001675 B000582 B001838
Tuesday, March 17, 1998	Received mouse/mice ID#AA13; A14-25 (CY + V3 loop) TLC image data.	B001797 B001838
Wednesday, March 18, 1998	Recorded a new litter of Tg mice; Received 1 mouse ID#AA20.	B001763-68; B001770; B001776-79; B001798; B1781-83 B001787-90; B001792-93 B001797
Thursday, March 19, 1998	Recorded a new litter of Tg mice; CK sick – half day off.	B001763-68; B001770; B001776-79; B001798; B1781-83 B001787-90; B001792-93 B001797
Friday, March 20, 1998	Recorded a new litter of Tg mice; CK sick- day off.	B001763-68; B001770; B001776-79; B001798; B1781-83 B001787-90; B001792-93 B001797
Saturday, March 21, 1998	Weekend; Analyzed data on A1-14 IP (-) Tg.	B001838
Sunday, March 22, 1998	Weekend	
Monday, March 23, 1998		
Tuesday, March 24, 1998	Received approval with revision for animal protocol amendment.	B001758-59

Wednesday, March 25, 1998		
Thursday, March 26, 1998		
Friday, March 27, 1998		
Saturday, March 28, 1998	Weekend	
Sunday, March 29, 1998	Weekend	
Monday, March 30, 1998	Conducted radioactive experiment; Obtained a new litter from Tg breeding.	B001763 B001766-68 B001776-79 B001798; B001782; B001787-90 B001793
Tuesday, March 31, 1998	Obtained a new litter from Tg breeding; Requested Alz. peptide synthesis; [Recorded monthly radioactivity (¹²⁵ I) disposal.*]	B001763, B001765 B001767-68 B001770 B001776-79 B001798, B001781 B001783; B001787-90 B001792 B00674
Wednesday, April 1, 1998		B001838
Thursday, April 2, 1998		B001838
Friday, April 3, 1998	Synthesis of requested peptides begun.	B001838 B001677 B000582
Saturday, April 4, 1998	Weekend; Synthesis of requested peptides completed.	B001678
Sunday, April 5, 1998	Weekend	
Monday, April 6, 1998	Requested animal protocol amendment for testing bio-distribution of labeled peptides/Antibodies.	B001746
Tuesday, April 7, 1998		
Wednesday, April 8, 1998		B001838
Thursday, April 9, 1998	Synthesized peptide purified; analyzed samples (control/DEAE cells or + inhibitor); Alz. Peptide (requested on March 31) synthesized.	B000675 B001679-82 B000586-89 B001836
Friday, April 10, 1998	Conducted radioactive experiment (10 th); Received an e-mail communication from Kathleen Morgan regarding termination.	
Saturday, April 11, 1998	Weekend; Analyzed electrophoresis	B001836

	images.	
Sunday, April 12, 1998	Weekend; Continued to analyze electrophoresis images.	B001836
Monday, April 13, 1998	Completed and signed Grant Application (PHS6246-1) "Catalytic Antibody to..."	B000313
Tuesday, April 14, 1998	Alz. peptide purified.	B000676
Wednesday, April 15, 1998	Obtained funding for SBIR Grant "Immunotherapy of Alzheimer's Disease".	
Thursday, April 16, 1998		
Friday, April 17, 1998	CK day off.	
Saturday, April 18, 1998	Weekend	
Sunday, April 19, 1998	Weekend	
Monday, April 20, 1998	Holiday	
Tuesday, April 21, 1998	Acquired image data onto Multi-Analyst application.	B001836
Wednesday, April 22, 1998		
Thursday, April 23, 1998		
Friday, April 24, 1998		
Saturday, April 25, 1998	Weekend	
Sunday, April 26, 1998	Weekend; Signed Animal Care Use Protocol Application "Production of Monoclonal Antibodies for..."	B001753-57
Monday, April 27, 1998		
Tuesday, April 28, 1998		
Wednesday, April 29, 1998		
Thursday, April 30, 1998	[Recorded monthly radioactivity (125I) disposal.*]	
Friday, May 1, 1998	Transgenic litter born (3 males, 1 female); treated ID#AA49, 50, 51, 53 with Alz-KLH.	B001763; B001765; B001767; B001768; B001770 B001776-79; B001798; B001781; B001783-84; B001787-90; B001792; B001797
Saturday, May 2, 1998	Weekend	
Sunday, May 3, 1998	Weekend	
Monday, May 4, 1998	Received approval for animal protocol update.	B001752
Tuesday, May 5, 1998		
Wednesday, May 6, 1998		

Thursday, May 7, 1998		
Friday, May 8, 1998		
Saturday, May 9, 1998	Weekend	
Sunday, May 10, 1998	Weekend	
Monday, May 11, 1998		
Tuesday, May 12, 1998		
Wednesday, May 13, 1998		
Thursday, May 14, 1998		
Friday, May 15, 1998		
Saturday, May 16, 1998	Weekend	
Sunday, May 17, 1998	Weekend; Created document on Alz. vaccine + risk.	B001836
Monday, May 18, 1998		
Tuesday, May 19, 1998		
Wednesday, May 20, 1998	Completed and signed Grant Application (PHS398) "Vaccine to Modulate..."	B000340
Thursday, May 21, 1998		
Friday, May 22, 1998		
Saturday, May 23, 1998	Weekend	
Sunday, May 24, 1998	Weekend	
Monday, May 25, 1998	Holiday	
Tuesday, May 26, 1998		
Wednesday, May 27, 1998	Completed and signed Grant Application (PHS398) "Probe to Visualize..."	B000366
Thursday, May 28, 1998		
Friday, May 29, 1998		
Saturday, May 30, 1998	Weekend	
Sunday, May 31, 1998	Weekend; [Recorded monthly radioactivity (¹²⁵ I) disposal.*]	
Monday, June 1, 1998		
Tuesday, June 2, 1998		
Wednesday, June 3, 1998		
Thursday, June 4, 1998		
Friday, June 5, 1998		
Saturday, June 6, 1998	Weekend	
Sunday, June 7, 1998	Weekend	
Monday, June 8, 1998	Ordered radioisotope (¹²⁵ I; 100 µCi).	
Tuesday, June 9, 1998	Transgenic litter born (1 male, 2 females).	B001763, B001765, B001767-68, B001770, B001776-79; B001798;

		B001781; B001783; B001787-90; B001792
Wednesday, June 10, 1999		
Thursday, June 11, 1999		
Friday, June 12, 1999		
Saturday, June 13, 1998	Weekend	
Sunday, June 14, 1998	Weekend	
Monday, June 15, 1998	Transgenic litter born (1 male, 8 females).	B001763, B001765; B001767-68; B001770-71; B001773; B001775, B001776-79; B001798, B001781, B001783, B001784, B001786-90, B001792, B001794 B001773, B001775
Tuesday, June 16, 1998		
Wednesday, June 17, 1998		
Thursday, June 18, 1998		
Friday, June 19, 1998	Transgenic litter born (2 males).	B001763, B001765, B001767, B001768, B001770, B001776-79; B001798, B001781; B001783; B001787; B001788-90; B001792
Saturday, June 20, 1998	Weekend	
Sunday, June 21, 1998	Weekend	
Monday, June 22, 1998	Filed 09/102,451 (issued Oct. 2000, Pat. 6,140,091).	
Tuesday, June 23, 1998		
Wednesday, June 24, 1998		
Thursday, June 25, 1998		

Friday, June 26, 1998		
Saturday, June 27, 1998	Weekend; Transgenic litter born (2 male, 1 female).	B001771; B001784, B001778, B001789, B001776 B001773; B001775, B001784; B001786 B001794
Sunday, June 28, 1998	Weekend	
Monday, June 29, 1998		
Tuesday, June 30, 1998	Analyzed Western blot image: R17/5A11; Recorded required inventory of radioisotopes; [Recorded monthly radioactivity (¹²⁵ I) disposal.*]	B001836 B001940 B001945-46
Wednesday, July 1, 1998		
Thursday, July 2, 1998	CK day off.	
Friday, July 3, 1998	Holiday	
Saturday, July 4, 1998	Weekend	
Sunday, July 5, 1998	Weekend	
Monday, July 6, 1998		
Tuesday, July 7, 1998		
Wednesday, July 8, 1998		
Thursday, July 9, 1998		
Friday, July 10, 1998		
Saturday, July 11, 1998	Weekend	
Sunday, July 12, 1998	Weekend	
Monday, July 13, 1998		
Tuesday, July 14, 1998	Filed animal protocol update for "Immunotherapy of Transgenic Alzheimer's..."	B001745
Wednesday, July 15, 1998	CK. half day-off; Received approval for animal protocol.	B001745
Thursday, July 16, 1998		
Friday, July 17, 1998		
Saturday, July 18, 1998	Weekend	
Sunday, July 19, 1998	Weekend	
Monday, July 20, 1998		
Tuesday, July 21, 1998		
Wednesday, July 22, 1998		
Thursday, July 23, 1998		
Friday, July 24, 1998		
Saturday, July 25, 1998	Weekend	
Sunday, July 26, 1998	Weekend	

Monday, July 27, 1998		
Tuesday, July 28, 1998		
Wednesday, July 29, 1998		
Thursday, July 30, 1998		
Friday, July 31, 1998		
Saturday, August 1, 1998	Weekend	
Sunday, August 2, 1998	Weekend	
Monday, August 3, 1998		
Tuesday, August 4, 1998		
Wednesday, August 5, 1998		
Thursday, August 6, 1998		
Friday, August 7, 1998		
Saturday, August 8, 1998	Weekend	
Sunday, August 9, 1998	Weekend	
Monday, August 10, 1998		
Tuesday, August 11, 1998	Requested brain morphology study; submitted tissue samples; [NOTE: Prior to this Vic Raso learned new skills associated with tissue histology including how to: dissect out or remove brain; fix using paraformaldehyde; transfer into series of sucrose solutions for dehydration; freeze tissue; use the cryostat for sectioning; prepare and use staining reagents such as thioflavin for histology; and relevant microscopy techniques.]	B001801
Wednesday, August 12, 1998		
Thursday, August 13, 1998		
Friday, August 14, 1998		
Saturday, August 15, 1998	Weekend	
Sunday, August 16, 1998	Weekend	
Monday, August 17, 1998		
Tuesday, August 18, 1998	Acquired images of Plaque 1 & Plaque 2.	B001940
Wednesday, August 19, 1998		
Thursday, August 20, 1998		
Friday, August 21, 1998		
Saturday, August 22, 1998	Weekend	
Sunday, August 23, 1998	Weekend; Received transgenic Tg 2576 mice; Received ID#AA24 mouse/mice.	B001761-62 B001797
Monday, August 24, 1998		
Tuesday, August 25, 1998		
Wednesday, August 26, 1998		
Thursday, August 27, 1998		

Friday, August 28, 1998		
Saturday, August 29, 1998	Weekend	
Sunday, August 30, 1998	Weekend	
Monday, August 31, 1998		
Tuesday, September 1, 1998	Holiday; Prepared Letter of Intent for Alz-related grant application.	B000432
Wednesday, September 2, 1998		
Thursday, September 3, 1998	Submitted Grant Application to Alzheimer's Association; Prepared Letter of Intent for 2 nd Alz-related grant application.	B000432-49 B000393
Friday, September 4, 1998	Submitted 2 nd Grant Application to Alzheimer's Association; Prepared Letter of Intent for 3 rd Alz-related grant application.	B000414 B000393-413
Saturday, September 5, 1998	Weekend	
Sunday, September 6, 1998	Weekend	
Monday, September 7, 1998	Holiday	B000414-431
Tuesday, September 8, 1998	Submitted 3 rd Grant Application to Alzheimer's Association; Requested female Tg mouse brain morphology study; Submitted tissue samples; Created KRS-AF document [??].	B001802 B001836
Wednesday, September 9, 1998	Revised and updated KRS document [??]	B001836
Thursday, September 10, 1998		
Friday, September 11, 1998		
Saturday, September 12, 1998	Weekend; Injected 4 mice with Alz-KLH/immunization.	B001770-71 B001804; B001809 B001810
Sunday, September 13, 1998	Weekend; Injected 3 mice with KLH alone as control.	B001770-71
Monday, September 14, 1998	Updated immunization documentation/records; Prepared documents for grant application: Alz-vaccine, risk, cerebral delivery.	B001763-64 B001836
Tuesday, September 15, 1998	Started to compile various documents for grant application.	B001836
Wednesday, September 16, 1998	Prepared grant documents: β -Amyloid Antibody figures.	B001836
Thursday, September 17, 1998		
Friday, September 18, 1998		
Saturday, September 19, 1998	Weekend	
Sunday, September 20, 1998	Weekend	
Monday, September 21, 1998		

Tuesday, September 22, 1998	Prepared brain sections for slides: Tg2576 mice with anti- β -Amyloid (5A11) vaccine.	B001602
Wednesday, September 23, 1998		
Thursday, September 24, 1998	Prepared for grant application: Edited "plaque" images.	B001836 B001940 B001942
Friday, September 25, 1998	Prepared for grant application: References, End of work plan.	B001836
Saturday, September 26, 1998	Weekend	
Sunday, September 27, 1998	Weekend	
Monday, September 28, 1998	Injected 6 Tg2576 mice; immunized 2 old Tg mice.	B001765-66 B001804 B001808
Tuesday, September 29, 1998		
Wednesday, September 30, 1998	Prepared Grant Application "Vaccine to modulate..."	B001836
Thursday, October 1, 1998	Revised Alz vector document (grant preparation)	B001836
Friday, October 2, 1998		
Saturday, October 3, 1998	Weekend; Edited plaque images.	B001940
Sunday, October 4, 1998	Weekend	
Monday, October 5, 1998		
Tuesday, October 6, 1998		
Wednesday, October 7, 1998		
Thursday, October 8, 1998		
Friday, October 9, 1998		
Saturday, October 10, 1998	Weekend; Analyzed Alz 14, 17, 40mer.	B001836
Sunday, October 11, 1998	Weekend; Finalized NIH Grant Application "Cerebral Delivery of..."	B000476-523
Monday, October 12, 1998	Holiday; Analyzed 5A11 6E2; 14, 17, 40mer.	B001836
Tuesday, October 13, 1998	Holiday	
Wednesday, October 14, 1998	Prepared Grant: Alz catalytic SBRI (unformatted).	B001836
Thursday, October 15, 1998		
Friday, October 16, 1998		
Saturday, October 17, 1998	Weekend	
Sunday, October 18, 1998	Weekend; Analyzed plaque images.	B001943-44
Monday, October 19, 1998		
Tuesday, October 20, 1998	Prepared Grant Application "Catalytic antibodies..."	B001836
Wednesday, October 21, 1998		
Thursday, October 22, 1998		
Friday, October 23, 1998	Acquired and analyzed images: Alz	B001834

	14, 17, 40mer.	
Saturday, October 24, 1998	Weekend; Repeated injection of Tg2576 mice ('boost').	B001767-68 B001804 B001809 B001810
Sunday, October 25, 1998	Weekend	
Monday, October 26, 1998		
Tuesday, October 27, 1998		
Wednesday, October 28, 1998		
Thursday, October 29, 1998		
Friday, October 30, 1998		
Saturday, October 31, 1998	Weekend	
Sunday, November 1, 1998	Weekend	
Monday, November 2, 1998		
Tuesday, November 3, 1998		
Wednesday, November 4, 1998		
Thursday, November 5, 1998		
Friday, November 6, 1998		
Saturday, November 7, 1998	Weekend	
Sunday, November 8, 1998	Weekend	
Monday, November 9, 1998		
Tuesday, November 10, 1998		
Wednesday, November 11, 1998	Holiday	
Thursday, November 12, 1998		
Friday, November 13, 1998		
Saturday, November 14, 1998	Weekend	
Sunday, November 15, 1998	Weekend	
Monday, November 16, 1998		
Tuesday, November 17, 1998		
Wednesday, November 18, 1998		
Thursday, November 19, 1998		
Friday, November 20, 1998		
Saturday, November 21, 1998	Weekend	
Sunday, November 22, 1998	Weekend	
Monday, November 23, 1998		
Tuesday, November 24, 1998		
Wednesday, November 25, 1998		
Thursday, November 26, 1998	Holiday	
Friday, November 27, 1998	Holiday	
Saturday, November 28, 1998	Weekend	
Sunday, November 29, 1998	Weekend	
Monday, November 30, 1998		
Tuesday, December 1, 1998		
Wednesday, December 2, 1998		
Thursday, December 3, 1998		
Friday, December 4, 1998		

Saturday, December 5, 1998	Weekend	
Sunday, December 6, 1998	Weekend	
Monday, December 7, 1998	Invention Disclosure "Immunological Approaches to Controlling β -Amyloid..."	
Tuesday, December 8, 1998	Requested Alz peptide synthesis (for making Alz-FF)	B000606
Wednesday, December 9, 1998	Prepared 'Sequence Report'.	B000607
Thursday, December 10, 1998		
Friday, December 11, 1998		
Saturday, December 12, 1998	Weekend	
Sunday, December 13, 1998	Weekend	
Monday, December 14, 1998		
Tuesday, December 15, 1998		
Wednesday, December 16, 1998		
Thursday, December 17, 1998	Requested Alz peptide synthesis (Alz-FF).	B000605
Friday, December 18, 1998		
Saturday, December 19, 1998	Weekend	
Sunday, December 20, 1998	Weekend	
Monday, December 21, 1998		
Tuesday, December 22, 1998		
Wednesday, December 23, 1998		
Thursday, December 24, 1998		
Friday, December 25, 1998	Holiday	
Saturday, December 26, 1998	Weekend	
Sunday, December 27, 1998	Weekend; Carried out calculations relating to Alz/Reduced peptide with KLH.	B000761
Monday, December 28, 1998		
Tuesday, December 29, 1998		
Wednesday, December 30, 1998		
Thursday, December 31, 1999		
Friday, January 1, 1999	Holiday	
Saturday, January 2, 1999	Weekend	
Sunday, January 3, 1999	Weekend	
Monday, January 4, 1999		
Tuesday, January 5, 1999	Prepared for experiment: calculations on peptide doses, volume etc.	B000760
Wednesday, January 6, 1999		
Thursday, January 7, 1999		
Friday, January 8, 1999		
Saturday, January 9, 1999	Weekend	
Sunday, January 10, 1999	Weekend	
Monday, January 11, 1999		

Tuesday, January 12, 1999	Torpey Assoc. compiled updated IP status related to Invention "Immunological Approaches to Controlling..."	
Wednesday, January 13, 1999		
Thursday, January 14, 1999		
Friday, January 15, 1999		
Saturday, January 16, 1999	Weekend	
Sunday, January 17, 1999	Weekend	
Monday, January 18, 1999		
Tuesday, January 19, 1999	Completed and signed NIH Grant Application "Immunotherapeutic Agents to Treat Alz..."	B000141
Wednesday, January 20, 1999		
Thursday, January 21, 1999	Conducted ELISA assays on Alz Tg mouse sera.	B001814-15
Friday, January 22, 1999		
Saturday, January 23, 1999	Weekend	
Sunday, January 24, 1999	Weekend	
Monday, January 25, 1999		
Tuesday, January 26, 1999		
Wednesday, January 27, 1999	Submitted NIH Grant Application "Novel Transition State Peptide Analog..."; Invention Disclosure "Immunological Control of..." sent from P. Torpey to Attorney.	B000524-69
Thursday, January 28, 1999		
Friday, January 29, 1999		
Saturday, January 30, 1999	Weekend	
Sunday, January 31, 1999	Weekend	
Monday, February 1, 1999	Attorney (KMF) studied invention disclosure; fax communication to V. Raso.	
Tuesday, February 2, 1999		
Wednesday, February 3, 1999		
Thursday, February 4, 1999		
Friday, February 5, 1999	Attorney (SYH) reviewed and summarized a list of comments & questions re. "Immunotherapy to reduce β -Amyloid..."	
Saturday, February 6, 1999	Weekend	
Sunday, February 7, 1999	Weekend	
Monday, February 8, 1999	Attorney (SYH) made initial analysis on patentability for invention.	
Tuesday, February 9, 1999		
Wednesday, February 10, 1999		

Thursday, February 11, 1999		
Friday, February 12, 1999		
Saturday, February 13, 1999	Weekend	
Sunday, February 14, 1999	Weekend	
Monday, February 15, 1999		
Tuesday, February 16, 1999		
Wednesday, February 17, 1999		
Thursday, February 18, 1999		
Friday, February 19, 1999		
Saturday, February 20, 1999	Weekend	
Sunday, February 21, 1999	Weekend	
Monday, February 22, 1999		
Tuesday, February 23, 1999	Attorney prepared a list of questions for V. Raso re. invention; Attorney (SYH) discussed patentability and non-obviousness with V. Raso.	
Wednesday, February 24, 1999		
Thursday, February 25, 1999		
Friday, February 26, 1999	Further discussion on non-obviousness issue (KMF & V. Raso).	
Saturday, February 27, 1999	Weekend	
Sunday, February 28, 1999	Weekend	
Monday, March 1, 1999	Attorney (SYH) reviewed fax communication from V. Raso re. obviousness argument; Began drafting claims; Attorney conference (SHY & KMF) re. claims.	
Tuesday, March 2, 1999	Received request from Attorney (SYH) for a copy of grant applications for preparing patent application; Discussed non-obviousness issue (SYH & Raso).	
Wednesday, March 3, 1999	Attorney (SYH) reviewed inventor's materials; continued with claim drafting.	
Thursday, March 4, 1999	Attorney (SYH) began drafting example section.	
Friday, March 5, 1999	Sent a copy of grant applications and other materials (data etc) to Attorney (SYH).	
Saturday, March 6, 1999	Weekend	
Sunday, March 7, 1999	Weekend	
Monday, March 8, 1999	Attorney (SYH) continued drafting example section from two grant applications.	

Tuesday, March 9, 1999	Attorney continued drafting and revising, adding new materials from inventor.	
Wednesday, March 10, 1999	Attorney (SYH) edited claims, studied prior art regarding patentability; Attorney (KMF) reviewed claims & example section.	
Thursday, March 11, 1999		
Friday, March 12, 1999		
Saturday, March 13, 1999	Weekend	
Sunday, March 14, 1999	Weekend	
Monday, March 15, 1999		
Tuesday, March 16, 1999		
Wednesday, March 17, 1999	Attorney (SYH) reviewed comments from Inventor; Communication with Inventor.	
Thursday, March 18, 1999	Attorney (SYH) edited example section; transmitted to Inventor; began drafting detailed description.	
Friday, March 19, 1999	Ordered radioisotope (^{125}I ; 10 mCi); Attorney (SYH) continued with detailed description.	
Saturday, March 20, 1999	Weekend	
Sunday, March 21, 1999	Weekend	
Monday, March 22, 1999	Attorney (SYH) continued with detailed description; drafted background of invention.	
Tuesday, March 23, 1999	Attorney (SYH) edited detailed description.	
Wednesday, March 24, 1999	Attorney (SYH) conference with Inventor regarding methods, additional claims, and results.	
Thursday, March 25, 1999	Attorney (SYH) revised detailed description; new materials provided from Inventor.	
Friday, March 26, 1999		
Saturday, March 27, 1999	Weekend; Requested peptide synthesis (Als1-40).	B000649
Sunday, March 28, 1999	Weekend	
Monday, March 29, 1999	Attorney (SYH) continued revising detailed description; new materials received from Inventor.	
Tuesday, March 30, 1999	Received radioisotope (^{125}I ; 10 mCi); Conducted radioactive experiment.	
Wednesday, March 31, 1999	Attorney (SYH) requested information from Inventor.	

Thursday, April 1, 1999		
Friday, April 2, 1999		
Saturday, April 3, 1999	Weekend	
Sunday, April 4, 1999	Weekend; Conducted radioactive experiment.	
Monday, April 5, 1999		
Tuesday, April 6, 1999		
Wednesday, April 7, 1999		
Thursday, April 8, 1999		
Friday, April 9, 1999		
Saturday, April 10, 1999	Weekend	
Sunday, April 11, 1999	Weekend	
Monday, April 12, 1999	Completed and signed NIH SBIR (PHS 6246-1) Grant Application, "Bispecific probe to visualize...).	B000450
Tuesday, April 13, 1999		
Wednesday, April 14, 1999		
Thursday, April 15, 1999	Attorney (SYH) contacted Inventor for materials.	
Friday, April 16, 1999		
Saturday, April 17, 1999	Weekend	
Sunday, April 18, 1999	Weekend	
Monday, April 19, 1999	Attorney (SYH) contacted Inventor for materials; Attorney conference (SYH & KMF) regarding status of patent application.	
Tuesday, April 20, 1999		
Wednesday, April 21, 1999		
Thursday, April 22, 1999	Attorney (SYH) requested information from Inventor.	
Friday, April 23, 1999		
Saturday, April 24, 1999	Weekend	
Sunday, April 25, 1999	Weekend	
Monday, April 26, 1999		
Tuesday, April 27, 1999	Recorded monthly radioactivity (¹²⁵ I) disposal.	
Wednesday, April 28, 1999		
Thursday, April 29, 1999		
Friday, April 30, 1999		
Saturday, May 1, 1999	Weekend	
Sunday, May 2, 1999	Weekend	
Monday, May 3, 1999		
Tuesday, May 4, 1999	Attorney (SYH) reviewed Inventor's comments and revised application accordingly.	
Wednesday, May 5, 1999		

Thursday, May 6, 1999		
Friday, May 7, 1999		
Saturday, May 8, 1999	Weekend	
Sunday, May 9, 1999	Weekend	
Monday, May 10, 1999		
Tuesday, May 11, 1999		
Wednesday, May 12, 1999	Attorney (SYH) revised example section according to Inventor's comments; prepared updated drafts for Pamela Torpey.	
Thursday, May 13, 1999	The updated draft copy mailed to Pamela Torpey.	
Friday, May 14, 1999		
Saturday, May 15, 1999	Weekend	
Sunday, May 16, 1999	Weekend	
Monday, May 17, 1999		
Tuesday, May 18, 1999		
Wednesday, May 19, 1999		
Thursday, May 20, 1999	Attorney (SYH) conference with Inventor regarding newly provided information; revised application.	
Friday, May 21, 1999	Attorney (SYH) edited application.	
Saturday, May 22, 1999	Weekend	
Sunday, May 23, 1999	Weekend	
Monday, May 24, 1999		
Tuesday, May 25, 1999	Attorney (SYH) drafted summary and abstract, transmitted to Inventor for review.	
Wednesday, May 26, 1999		
Thursday, May 27, 1999		
Friday, May 28, 1999		
Saturday, May 29, 1999	Weekend	
Sunday, May 30, 1999	Weekend	
Monday, May 31, 1999		
Tuesday, June 1, 1999		
Wednesday, June 2, 1999		
Thursday, June 3, 1999		
Friday, June 4, 1999		
Saturday, June 5, 1999	Weekend	
Sunday, June 6, 1999	Weekend	
Monday, June 7, 1999		
Tuesday, June 8, 1999		
Wednesday, June 9, 1999		
Thursday, June 10, 1999	FedEx from Attorney to Inventor (contents unspecified in billing record).	

Friday, June 11, 1999		
Saturday, June 12, 1999	Weekend; Conducted radioactive experiment.	
Sunday, June 13, 1999	Weekend	
Monday, June 14, 1999	Attorney (SYH) conference with Inventor regarding application; revised application for filing.	
Tuesday, June 15, 1999	Fax sent from Attorney to Inventor (contents unspecified in billing record).	
Wednesday, June 16, 1999	Provisional application filed, "Immunological control of β -Amyloid...".	
Thursday, June 17, 1999	Attorney's postage and photocopy charges on billing record.	
Friday, June 18, 1999		
Saturday, June 19, 1999	Weekend; Ordered radioisotope (^3H ; 250 μCi).	
Sunday, June 20, 1999	Weekend	
Monday, June 21, 1999		
Tuesday, June 22, 1999		
Wednesday, June 23, 1999		
Thursday, June 24, 1999		
Friday, June 25, 1999		
Saturday, June 26, 1999	Weekend	
Sunday, June 27, 1999	Weekend	
Monday, June 28, 1999	Attorney's postage and photocopy charges on billing record.	
Tuesday, June 29, 1999		
Wednesday, June 30, 1999	Recorded required inventory of radioisotopes.	
Thursday, July 1, 1999		
Friday, July 2, 1999		
Saturday, July 3, 1999	Weekend	
Sunday, July 4, 1999	Weekend	
Monday, July 5, 1999		
Tuesday, July 6, 1999		
Wednesday, July 7, 1999		
Thursday, July 8, 1999		
Friday, July 9, 1999	Received request for a copy of grant application under Freedom of Information Act.	
Saturday, July 10, 1999	Weekend	
Sunday, July 11, 1999	Weekend	
Monday, July 12, 1999		
Tuesday, July 13, 1999		

Wednesday, July 14, 1999		
Thursday, July 15, 1999		
Friday, July 16, 1999		
Saturday, July 17, 1999	Weekend	
Sunday, July 18, 1999	Weekend	
Monday, July 19, 1999	Notarized "Human Compatible Vaccines for treating Alzheimer's..." (conception).	B000130
Tuesday, July 20, 1999		
Wednesday, July 21, 1999		
Thursday, July 22, 1999		
Friday, July 23, 1999	Requested peptide synthesis (Alz.1-42).	B000633
Saturday, July 24, 1999	Weekend	
Sunday, July 25, 1999	Weekend	
Monday, July 26, 1999		
Tuesday, July 27, 1999	Injected (IFA) Tg mice "AA-49/50".	B000750
Wednesday, July 28, 1999		
Thursday, July 29, 1999		
Friday, July 30, 1999		
Saturday, July 31, 1999	Weekend	
Sunday, August 1, 1999	Weekend	
Monday, August 2, 1999		
Tuesday, August 3, 1999		
Wednesday, August 4, 1999		
Thursday, August 5, 1999		
Friday, August 6, 1999		
Saturday, August 7, 1999	Weekend	
Sunday, August 8, 1999	Weekend	
Monday, August 9, 1999		
Tuesday, August 10, 1999		
Wednesday, August 11, 1999	Injected 3 mice "Alum + AB40".	B000745
Thursday, August 12, 1999		
Friday, August 13, 1999	Completed and signed NIH SBIR(II) Grant Application (PHS 6246-2), "Immunotherapy of Alzheimer's disease".	B000187
Saturday, August 14, 1999	Weekend	
Sunday, August 15, 1999	Weekend	
Monday, August 16, 1999		
Tuesday, August 17, 1999		
Wednesday, August 18, 1999		
Thursday, August 19, 1999		
Friday, August 20, 1999		
Saturday, August 21, 1999	Weekend	

Sunday, August 22, 1999	Weekend	
Monday, August 23, 1999		
Tuesday, August 24, 1999		
Wednesday, August 25, 1999		
Thursday, August 26, 1999		
Friday, August 27, 1999		
Saturday, August 28, 1999	Weekend	
Sunday, August 29, 1999	Weekend	
Monday, August 30, 1999		
Tuesday, August 31, 1999		